COMPARISON OF INTRATHECAL NALBUPHINE VS FENTANYL ADDED TO 0.5% HYPERBARIC BUPIVACAINE FOR PERIOPERATIVE ANAESTHESIA AND PERIOPERATIVE / POST OPERATIVE ANALGESIA IN HERNIOPLASTY

DISSERTATION SUBMITTED TO THE TAMILNADU

DR.M.G.R. MEDICAL UNIVERSITY, CHENNAI

In partial fulfilment of the requirements for the degree of

M.D. BRANCH – X

(ANAESTHESIOLOGY)

DEPARTMENT OF ANAESTHESIOLOGY

TIRUNELVELI MEDICAL COLLEGE HOSPITAL

TIRUNELVELI – 627011

MAY-2019

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PROTOCOL TITLE: COMPARISON OF INTRATHECAL NALBUPHINE VS FENTANYL ADDED TO 0.5% HYPERBARIC BUPIVACAINE FOR PERIOPERATIVE ANAESTHESIA AND PERIOPERATIVE / POST OPERATIVE – ANALGESIA IN HERNIOPLASTY
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Dear Dr.A.GOVISHKAMAL, MBBS, The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during The IEC meeting held on 15.12.2017.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of The Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of The validity
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5. The TIREC will monitor The study
6. At The time of PI's retirement/leaving the institute, The study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
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   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in The original project. (Page no. Clause no. etc.)
   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and The revised budget form should be submitted.
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, The same should be documented.
   d. If there are any amendments in The trial design, These must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of The IEC, only then can they be implemented.
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CONTENTS

INTRODUCTION

In 1898, August Bier first described "cocainisation of the spinal cord". The technique has been refined over the years and has evolved into the modern concept of intrathecal, spinal or subarachnoid block. One of the most commonly performed technique in modern anaesthesia is Central neuraxial blockade.

In surgeries like hernioplasty the most preferred regional anaesthesia is spinal anaesthesia. Spinal anaesthesia produces dense motor, sensory and sympathetic blockade. Subarachnoid block is a preferred technique in patients who are prone to aspiration like obesity, full stomach, GERD and in patients with reduced respiratory drive. Spinal anaesthesia reduces mortality and morbidity in high risk surgical patients.

Simplicity to perform and more rapid onset with good sensory as well motor block[1], excellent analgesia and decreased stress response to surgery and intra operative blood loss have made spinal anaesthesia preferable in infraumbilical surgeries like hernioplasty. Most commonly used amide local anaesthetic bupivacaine produces prolonged intense sensory and motor block with significant sympathetic blockade and excellent surgical relaxation[2, 3]. Normally, spinal anaesthesia with hyperbaric bupivacaine lasts for 2 to 2.5 hours[4]. Commonly used dosage, it produce more undesirable side effects[5]: By reducing the dosage of

bupivacaine, limits its distribution of spinal block, and it causes comparably rapid recovery[6].

Various adjuvants are added to the local anaesthetics intrathecally, to prolongate the duration of anaesthesia. Adjuvants not only reduce the undesirable hemodynamic effects of spinal anaesthesia, by lowering the requirement of local anaesthetic dose, but also provide satisfactory block[7,8].

Among the adjuvants the most commonly preferred are the opioids. These adjuvants have "synergistic anti-nocioceptive effect" along with intrathecal local anaesthetic both during intra operative and post operative periods by extending analgesia duration[9]. Opioids act at the receptor site in the spinal cord[10] and the local anaesthetics have their action at the spinal nerve axon.

In 1979, Wang and his colleagues[11] first used intrathecal opioids for acute pain treatment. Since then, intrathecal opioid is widely used to increase the quality of Intraoperative anaesthesia, prolong the postoperative analgesia, traumatic and chronic cancer pain. Administration of intrathecal opioid along with local anaesthetics is to improve the quality of analgesia and to decrease the requirement of postoperative analgesics[12].

Various opioids have been used intrathecally like morphine, fentanyl, buprenorphine and nalbuphine to fasten the onset and prolong the duration of sensory and motor blockade.

Nalbuphine is synthetically prepared opioid. It has both κ agonist and μ antagonist properties[13]. When given intrathecally it binds to kappa receptors in the spinal cord and brain. It produces analgesia and sedation via kappa receptors and hence there is no adverse effects mediated by μ receptors. Side effects like shivering, nausea, vomiting and urinary retention are infrequent with nalbuphine hydrochloride. Nalbuphine reaches ceiling effect at lower intrathecal dosage and so no need to increase the dosage.

Fentanyl is a lipophilic μ receptor opioid agonist. Intrathecal fentanyl as adjuvant to local anaesthetic has a rapid onset of action and significantly reduces visceral and somatic pain which have been proved in various studies[14, 15].

Although there are several studies that includes comparison of Nalbuphine and fentanyl as adjuvant, there is no particular study in patients undergoing hernioplasty.

In this study we compared the effectiveness of the two adjuvants nalbuphine and fentanyl added to 0.5% hyperbaric bupivacaine in patients undergoing hernioplasty as Group A and Group B respectively, along with a control group C of intrathecal bupivacaine alone with normal saline.

SUBARACHNOID BLOCK

Anatomy

Predictable sympathetic blockade, sensory analgesia or anaesthesia and motor blockade are produced by central neuraxial blockade. It mainly depends on the dose, volume and concentration of local anaesthetic injected into subarachnoid space. To perform the technique of spinal anaesthesia three dimensional understanding of anatomy is must.

The vertebral(spinal) canal, a bony structure that extends from the foramen magnum to the sacral hiatus. The spinal cord and its nerve roots are contained within the vertebral (spinal) canal. True vertebra consists of C1-7 cervical, T1-12 thoracic and L1-5 lumbar vertebrae. The false vertebra consists of the sacrum 5 fused segments and the coccyx 4 fused segments.

There are four curvatures present in our adult spine. The major importance of these curvatures are its major role in the distribution of local anaesthetic solution in subarachnoid space. Vertebrae held together by Intervertebral discs and series of overlapping ligaments.[16,17] fig.1

The ligaments are namely:

1 **Supraspinous ligament:**

It connects the tip of each spinous process to the other.

2 **Interspinous ligament:**

It connects the vertebral spines

3 Ligamentum flavum :

It connects the lamina above and below

4 Anterior Longitudinal Ligament:

It Connects the front (anterior) of the vertebral body to the front of the annulus fibrosus.

5 Posterior Longitudinal Ligament:

It connects the back (posterior) of the vertebral body to the back of the annulus fibrosus.

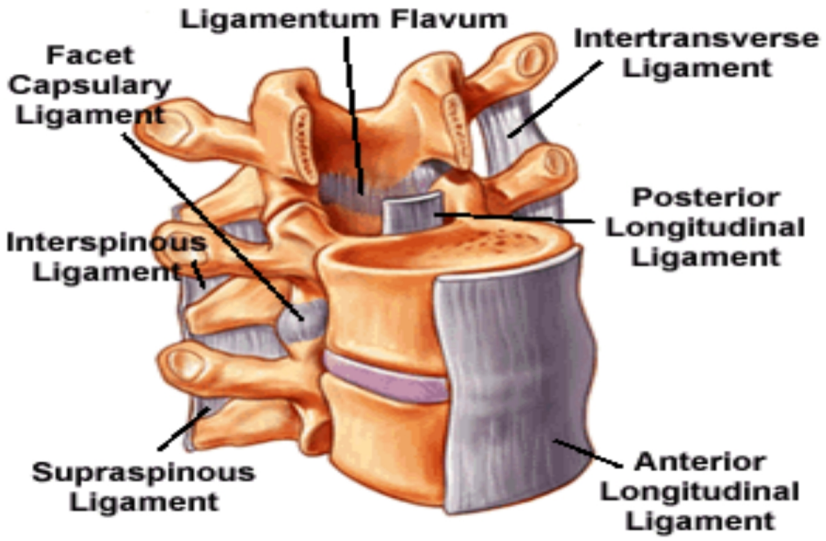

Fig.1 VERTEBRAL LIGAMENTS.

Common palpable landmark that may corresponds to particular level includes:

1. The most prominent spinous process in the cervical region - corresponds to the 7^{th} cervical vertebra.

2. Inferior angle of scapula usually corresponds to the seventh thoracic vertebra and
3. The most important landmark used to determine the level for insertion of spinal needle is Tuffier line.

Tuffier line: The line connecting the two iliac crests almost crosses the vertebral column at the level of intervertebral space of fourth and fifth lumbar vertebra.

Contents of Intervertebral canal are[18]:

1. Roots of spinal nerves
2. Spinal membrane with the spinal cord and cerebrospinal fluid
3. Vessels, fat and areolar tissue

Spinal cord begins from the rostral border of the medulla at the upper border of atlas it begins and ends distally in the conus medullaris.[18,19,20]

There is differential growth rates between bony vertebral canal and spinal cord. The cord terminates much higher than the bony canal.

Foetus: Length of cord Varies occupies entire canal length.

Infants: upto L3 level

Adult : upto lower border of L1.

Below the conus, the roots oriented parallel to axis and resemble a horse's tail, from which the name cauda equina is derived.

The spinal cord is surrounded by three layers of connective tissue known as the meninges :

- Duramater
- Arachnoid mater
- Piamater

Duramater is a tough fibro elastic membrane. It is attached to margins of foramen magnum above as an extension of cranial dura and ends at lower border of the S2 sacral vertebra. The investing layer of duramater is pierced by the anterior and posterior nerve roots from the spinal cord.

The arachnoid mater is a thin transparent sheath. It is closely adherent to inner surface of the dura, imparts impermeability. It serves as the major pharmacologic barrier and prevents movement of drug from the epidural to the subarachnoid space.

The piamater is a highly vascular layer. It is closely adherent to the cord. It sends delicate septa into its substances. Filum terminale (prolongated inferior end of piamater) penetrates the distal end of dural sac and is attached to the periostium of coccyx.

The subarachnoid space lies between the arachnoid matter and the piamater. Subarachnoid space is filled with the cerebrospinal fluid. Cerebrospinal fluid is formed from the choroid plexus of lateral, third and fourth ventricle. It contains the spinal nerve roots and the denticulate

ligament. Lumbar puncture is done below the L2 vertebra to L3-L4 interspace.It is done at this level to prevent damage to spinal cord.

The spinal cord get its blood supply by three longitudinal arterial channels:

- One anterior spinal artery.
- Two posterior spinal arteries the spinal cord.

Vertebral arteries are main contributers to the spinal arteries. It reaches only till the cervical segment of the cord. Posterior spinal arteries emerge from the cranial vault and it supplies the dorsal (sensory) portion of the spinal cord and have rich collateral anastomotic
links from the subclavian and intercostal arteries, this area of the spinal cord is relatively protected from ischemic damage. The spinal arteries also receive blood through radicular arteries which accompanies the roots of spinal nerves.

Among these radicular arteries only few are larger in size. Arteria radicularis magna, or artery of Adamkiewicz, which is a highly variable artery arises from the aorta in the lower thoracic or upper lumbar region. It supplies blood to the lower two-thirds of the spinal cord. Injury of arteria radicularis magna will cause anterior spinal artery syndrome. Thrombosis in any of the anterior and posterior spinal arteries will cause spinal cord infarction since they don't have any anastomosis. Venous drainage of spinal cord by six longitudinal venous channels.

- Two paired anterolateral and posterolateral channels
- Unpaired anteromedian and posteromedian venous channels

Unpaired and paired venous channels forms venous plexus. Venous blood drains from here via radicular veins into segmental veins.. These veins prominent in the lateral epidural space and empty into the azygos venous system.

SPINAL NERVES

Nerve roots merge to form 31 pairs of spinal nerves (8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 1coccygeal) distal to dorsal root ganglion. The sensory fibers traverse the posterior aspect of the subarachnoid space, so they tend to lie dependent in a supine patient, and thus making them particularly vulnerable to hyperbaric solutions (heavier than CSF) containing local anaesthetic. The dura traverses this area and becomes thinned (often called the dural sleeve), thereby facilitating penetration of local anaesthetic. Spinal block by local anaesthetics occurs by blockade of sodium ion conductance in this region.

PHYSIOLOGY

CSF Circulation

Cerebrospinal fluid described by Galen as colorless fluid filling the ventricles. The choroid plexus in the ventricles as the site of production of CSF was first described by WEED. CSF is secreted at rate of 0.3 to 0.5ml/min. The average volume ranges from 120 to 150 ml, and it is in cerebral subarachnoid space- 25ml,in the ventricles-35ml and spinal subarachnoid space -75ml

CSF Pathways

Cerebrospinal fluid transverses from the lateral ventricles into the third ventricle through foramen of monro and from there in to the fourth ventricle through the aqueduct of sylvius. From the fourth ventricle it reaches the subarachnoid space through the median foramen of magendie and the lateral foraminae of Luschka. The cerebral ventricles and the subarachnoid space has functional communication only at the fourth ventricle. It bathes Brain and spinalcord.

CSF Absorption

The absorption of CSF is a dual process, being chiefly a rapid drainage through arachnoid villi, and arachnoid granulations of superior sagittal sinus and its lateral lacunae into the great dural sinuses with small contribution through a slow escape into the true lymphatic vessels by a

perineural course. About 300-380 ml of CSF enters venous circulation per day.

Physical properties of CSF are:

pH: 7.32

Specific gravity at body temperature: 1.002-1.009

Specific gravity at 4 degree Celsius: 1.0003

Density: 1.0003gm/ml

Baricity: 1.000

CSF pressure: 50-180mm of H20

Spinal anaesthesia was introduced by AUGUST BIER in 1898.

Subarachnoid block produces:

- Sympathetic blockade
- Sensory blockade
- Motor blockade

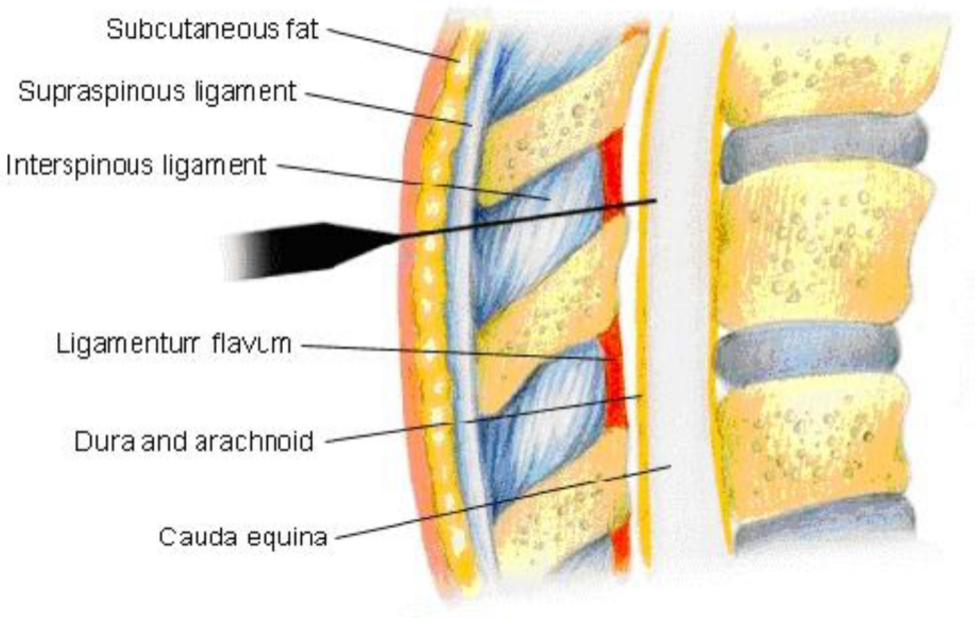

Fig.2. Structures pierced by spinal needle

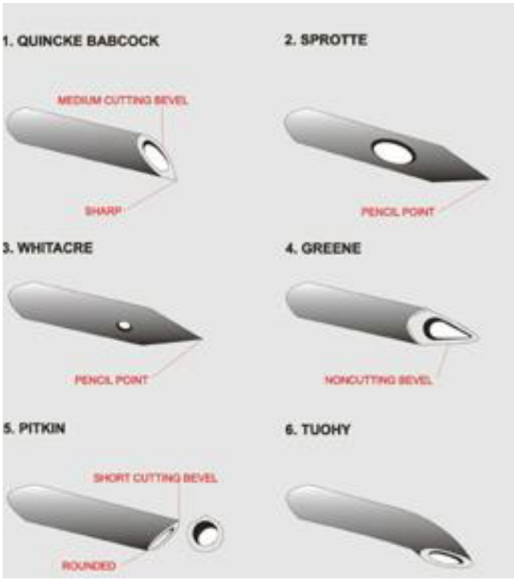

Fig.3.Spinal needles

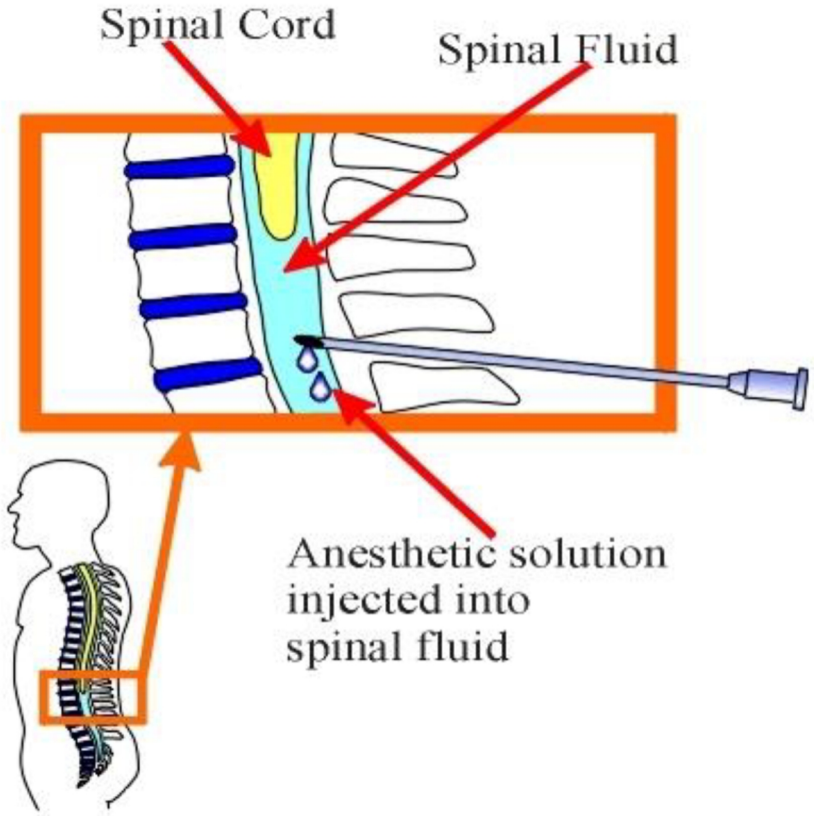

Fig.4.Site of injection of Drug

BLOCK LEVEL REQUIREMENTS

Surgery Level required

Lower segment Cesarean section, Gynecological surgeries, Intestinal surgery	T6
Hernioplasty/Urological surgeries :Transurethral resection of prostate(TURP)/bladdertumor(TURB)	T10
Knee surgeries	L1
Foot and ankle surgeries	L2
Perineal and anal surgeries	S2-S4

ADVANTAGES OF SUBARACHNOID BLOCK

- Patient is conscious during surgery
- Lower incidence of Nausea/Vomiting/sore throat
- Pain Control
- ↓incidence of DVT.

Indications of subarachnoid block

- Obstetric procedures.
- Gynecological procedures.
- Lower abdominal surgeries.

Orthopaedic surgery- all lower limb surgeries & few pelvic surgeries

Contraindications of subarachnoid block

Absolute contraindications:

Patient refusal.

Hypovolemia.

Increased intracranial pressure

Infection at the site of injection

Coagulopathy.

Indeterminate neurologic disease

Relative contraindications:

Major spine deformities or previous spine surgeries.

Certain cardiac diseases if level above T6 are required.

Unknown duration of surgery

Infection distant from anatomic site of puncture.

POSITIONING

For technical ease and successful block proper positioning is very important.

The various positions are

1. Lateral decubitus
2. Sitting (Fig.5)

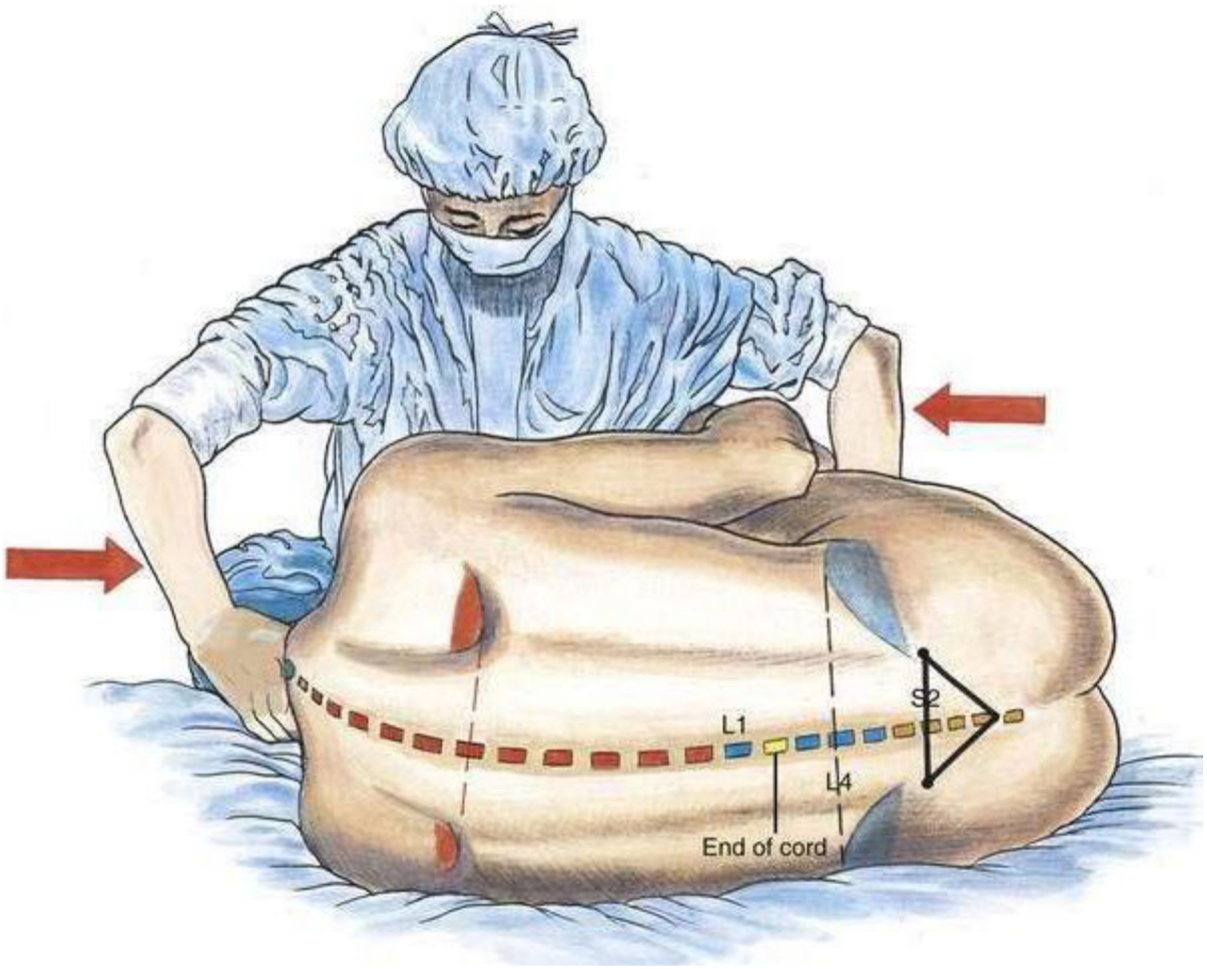

Fig.5 Positioning for spinal anaesthesia

Fig.6.sitting position

3. Prone (using hypobaric drug)

APPROACH

The different approaches are

1. Midline approach

In midline approach the needle is introduced in midline and is directed slightly cephalad and piercing the supraspinous ligament and the ligamentum flavum is felt by popups.Then the needle advancement pierces the dura and then subarachnoid membrane as signalled by free flowing CSF. Free flowing CSF is the best sign of correct lumbar puncture.

2. Lateral or Paramedian approach

This approach is indicated in patients with positioning difficulty (Kyphoscoliosis, Sclerotic lesions). In this approach the needle is inserted 1cm lateral and 1cm caudal to the inferior aspect of spinal process.

Fig.7.Lateral approach

3. Taylor's approach

Paramedian type of technique. In this approach the needle is directed towards L5-S1 space and needle entry should be 1cm medial and 1cm inferior to posterior superior iliac spine. Taylor's approach is used in conditions of lumbar spine deformity.

Factors determining local anaesthetic spread21

Properties of local anaesthetics

- Baricity
- Dose
- Volume
- Specific gravity
- Concentration

Patient Characteristics

- Height of the patient
- Position of the patient during & after injection
- Spinal column anatomy

Cerebrospinal fluid Characteristics

- Cerebrospinal fluid composition
- CSF volume

Complications of spinal anaesthesia

- High/ total spinal anaesthesia

- Failed spinal
- Patchy block or inadequate block
- Intravascular injection
- Neurotoxicity & neurological damage.
- PPDH-Postdural puncture headache
- Cardiovascular disturbances like hypotension, bradycardia.
- Back pain
- Arachanoiditis
- Cauda equine syndrome

Ratio between the density of a local anaesthetic solution at a specific temperature, to the density of CSF at the same temperature is known as BARICITY. BARICITY determines the spread and distribution of local anaesthetics in the CSF.

Baricity of less than 1 relative to CSF are Hypobaric solutions. Hypobaric solutions are best choice for procedures in perineal or in prone jack knife positions. Baricity equal to 1 are Isobaric solutions. Patient positioning andGravity does not play a role in the spread of Isobaric local anaesthetics.

Baricity more than 1 relative to CSF are Hyperbaric solutions. Hyperbaric solutions are denser than CSF. Patient positioning and Gravity affect the spread of Hyperbaric local anaesthetics.

Local Anaesthetics :

Local anaesthestics when injected into the CSF, it bathes nerve root in the subarachanoid space. Blockade of conduction in posterior nerve root fibres interrupts the somatic & visceral sensation. Blockade of anterior nerve root prevents efferent motor & autonomic outflow. Potency of the drug, onset and duration of anaesthesia and its side effects determines the choice of local anaesthetics. Rate of removal of local anaesthetics from spinal cord tissue is determined by blood supply to the spinal cord tissue. vascular absorption eliminates local anaesthetics from epidural space & subarachnoid space. Faster the blood flow to spinal cord, more rapid is the elimination of local anaesthetics.

OPIOIDS AND OPIOID RECEPTORS

Opioid derived from Greek word "*opos"* means juice. Any substance which acts on **"**Opioid receptors" and produces morphine like effects, that blocked by antagonists such as naloxone, regardless of its origin/structure is an Opioid. Opioid includes natural, semi synthetic and synthetic agents.

From the juice of *Papaver somniferous, the* natural alkaloids opiates like morphine, thebaine and codeine are derived.

Fig.8. Papaver somniferum

ENDOGENOUS OPIOIDS

Opioids found within the brain are endogenous opioids, which acts through opioid receptor. Primarily there are three classes - enkephalins, endorphins, and dynorphins.

CLASSIFICATION

NATURAL - Morphine, Codeine, Thebaine

SEMI SYNTHETIC - Dihydromorphone, Heroin ,Oxymorphone

SYNTHETIC - Pentazocine, Pethidine, Fentanyl, Buprenorphine, Nalbuphine etc.,

Uses of opioids:

1. For Analgesia (intraoperative and postoperative)
2. Used for premedicantion
3. Used as an Induction agent
4. Used for Sedation in ICU
5. Used to prevent and control shivering
6. Used as an adjuvant to local anesthetic in subarachnoid block/Epidural.

Opioid Receptors:

Opioid receptors primarily mediate analgesic, and other effects of opioid drugs (like morphine) and endogenous opioid peptides. belongs to the G protein-coupled receptor family. Inhibition of adenylate cyclase[22],

and reduction of cellular cyclic adenosine monophosphate content are mediated by them.

SUB TYPES OF OPIOID RECEPTORS

Opioid receptors[23] are subdivided into three subtypes. They are : mu(μ), kappa(κ), delta(δ).

mu(μ) receptors - gene on chromosome 6. They are subdivided into μ1, μ2, μ3.

μ1 : mediates analgesia and physical dependence.

μ2 : mediates respiratory depression,miosis, constipation, euphoria.

μ3 : vasodilation,increase GH and prolactin secretion.

kappa(κ) receptors - gene on chromosome 8.

They are subdivided into κ 1, κ 2, κ 3.

They mediates analgesia, dysphoria, miosis, sedation, diuresis.

delta(δ) receptors - gene on chromosome 1 and 4.

They mediates analgesia, respiratory depression, dependence.

Newer opioid receptors

Nociceptin receptor

Zetta receptor.

Based on receptor interaction opioids are classified:

1. Pure agonist (+),
2. Mixed agonist / antagonist (+/-) and
3. Pure Antagonist (-).

In Spinal

Their action is in substantia gelatinosa of dorsal horn cells. Inhibition of substance P release. Inhibition of the ascending transmission of nociceptive stimuli.

Peripheral mechanisms

1. Stimulates G protein synthesis and increase cAMP which causes
2. Raises K+ - Hyperpolarization of membrane
3. Diminished Ca2+ - Excitability

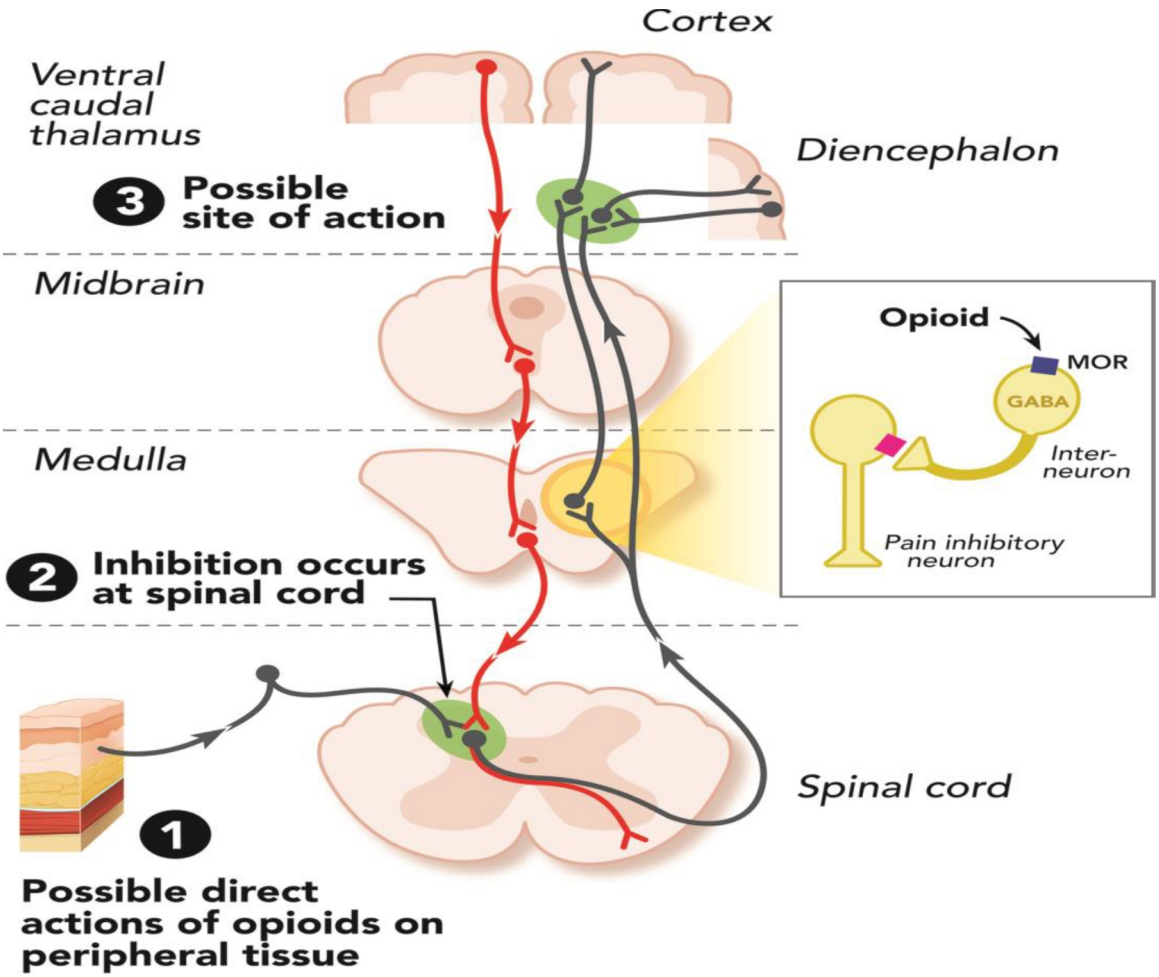

Fig.9. Site of action of opioids

PHARMACOLOGY OF FENTANYL[24, 25]

Synthetic opioid receptor agonist. Comparatively fentanyl is 75-125 times more potent than morphine.

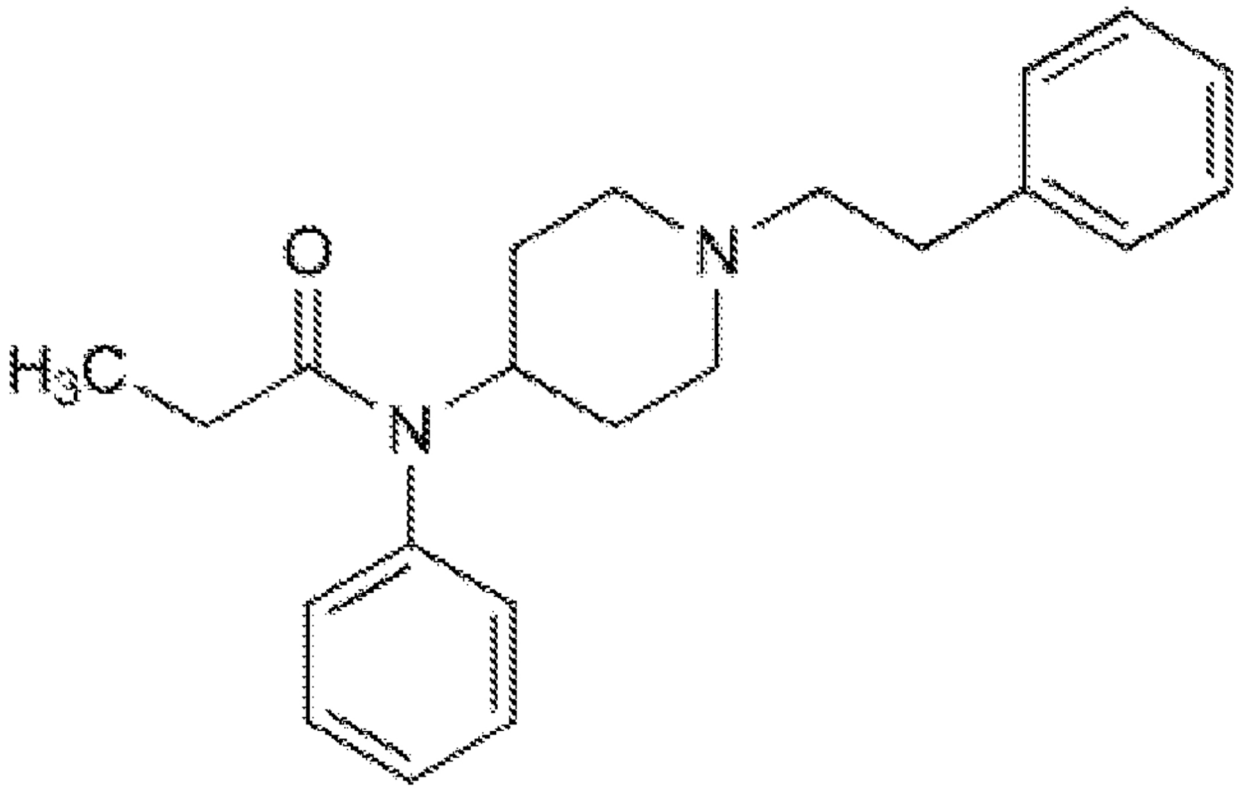

Fig.10.chemical structure of fentanyl

Chemical structure of fentanyl

Fentanyl is PHENYL PHERIDINE DERIVATIVE with nucleus containing PHENANTHERENE structure as in fig.9

Mechanism of action:

Fentanyl is highly lipophilic synthetic compound. It has pure agonist action on stereotypic μ type opioid receptor, both at presynaptic and post synaptic sites of central nervous system and peripheral tissue. Fentanyl cause presynaptic inhibition of neurotransmitter (Ach, Dopamine,

Norepinephrine, substance P) release, by increasing potassium conductance and by calcium channel inactivation.

Fentanyl also inhibits the release of excitatory neurotransmitter like substance P. Effect is produced by inhibiting adenylcyclase hence decrease neurotransmitter release.

Dose and mode of administration

Fentanyl is a major component of balanced anaesthesia

- 1-2mcg/kg for intravenous analgesia
- 25mcg (maximum) for intrathecal
- 5-20mcg/kg for oral/transmucosal
- 75-100mcg/hr for transdermal

The plasma concentration of fentanyl should be around **20-30ngm/ml** for maximum analgesia.

Pharmacokinetics

Fentanyl is very highly lipophilic, so crosses the blood brain barrier easily, hence it has rapid onset of action and greater potency. Volume of distribution is very high & hence it is very short acting. Fentanyl gets rapidly distributed to fat, skeletal muscles and pulmonary tissue. With continuous infusion or multiple dosages the saturation of tissue occurs & it will produce prolonged duration of action. Intrathecally given fentanyl produces selective segmental analgesia, by blocking opioid receptors of dorsal horn. Duration and amount of analgesia depends upon the drug

concentration. Lower dose of fentanyl is required for intrathecal administration than the systemic dosage & so the side effects are minimal. But some systemic side effects do occur, it's because of cephalad migration of drug and vascular or tissue uptake. Fentanyl is smaller molecule and lipophilic hence readily crosses placenta.

pKa of fentanyl —8.4, Protein binding-80%, Clearance-1530ml/min, Volume of distribution- 335litres, Elimination half-life- 31.66 hrs Context sensitive half-life after 4 hours of infusion- 260 minutes.

Metabolism

90% of fentanyl is metabolized in liver by N-Demethylation to produce Norfentanyl, hyroxy proprionyl fentanyl, hyroxy Proprionyl nor fentanyl. These products are minimally active.

Excretion

Excretion is mainly by kidneys. Only 10% is excreted unmetabolized. Metabolites are seen in urine even after 72 hrs.

Elimination half life

80% of the drug eliminates from plasma in less than 5 minutes as it is highly lipid soluble. The plasma concentration is reached only by redistribution hence it has a longer half life.

Context sensitive half life

Half life is prolonged if the drug is given as infusion for greater than 2 hrs as the peripheral tissues become saturated.

Pharmacodynamics

Central Nervous System

Rapid IV injection of fentanyl may produce seizure like activity. On EEG monitoring they were found to be myoclonus due to inhibition neurons of temporal lobe. It produces skeletal muscle rigidity. At normal Paco2, it produces rise in intracranial pressure by 6-9mmhg associated with fall in mean arterial pressure(MAP) and cerebral perfusion pressure due to autoregulatory reduction in cerebral vascular resistance. Muscle rigidity caused by μ receptors of brain stem, midline nuclei and basal ganglia.

Cardiovascular System

Fentanyl given in high dose depresses isolated myocardial contractility, but at normal dose it does not produce direct myocardial depression. Fentanyl markedly depresses the Carotid sinus baroreceptor reflex control of heart rate. Fentanyl does not cause histamine release as with other opioids such as morphine or pethidine. Fentanyl has vagomimmetic action and it produces dose dependent fall in heart rate, even cause severe bradycardia or asystole is noted at high doses. It suppress the central sympathetic outflow & it produces dose dependent fall in blood pressure.

Respiratory System

Fentanyl produces dose dependent suppression of respiratory centre & cause reduction in tidal volume and minute ventilation. Redistribution of the drug from the peripheral tissue may cause severe delayed respiratory depression in the post-operative period.

Gastrointestinal System

Fentanyl decreases gastrointestinal motility & hence causes constipation. Fentanyl by direct stimulation of chemoreceptor trigger zone, produces nausea and vomiting.

Pruritis

Fentanyl produces intense pruritis which seems to be mediated by μ type opioid receptor.

Uses of fentanyl:

- Used for sedation in ICU setup
- Used for Surgical analgesia
- Used along with inhalation agents in balanced anaesthesia
- Very high dose in IHD patients as induction
- Used for blunting intubation stress response
- Used as adjuvant in regional anaesthesia

Adverse Effects of fentanyl:

Persistent respiratory depression or recurrent respiratory depression in post operative periods, prominent fall in heart rate(HR), fall in blood pressure, rigidity and myoclonus, raised Intracranial pressure, reflex coughing

PHARMACOLOGY OF NALBUPHINE

To overcome the abuse potential, many synthetic opioids were developed. Those synthetic opioid substances are referred to as mixed agonist-antagonist analgesics. Nalbuphine comes under them.

CHEMISTRY

Nalbuphine hydrochloride,is a synthetic narcotic agonist-antagonist analgesic of phenanthrene series. Chemically, nalbuphine is related to the opioid antagonist naloxone and opioid agonist oxymorphone. Nalbuphine hydrochloride is soluble in water at 25^0C, ethanol 0.8% and available only as an injectable solution.

CHEMICAL STRUCTURE

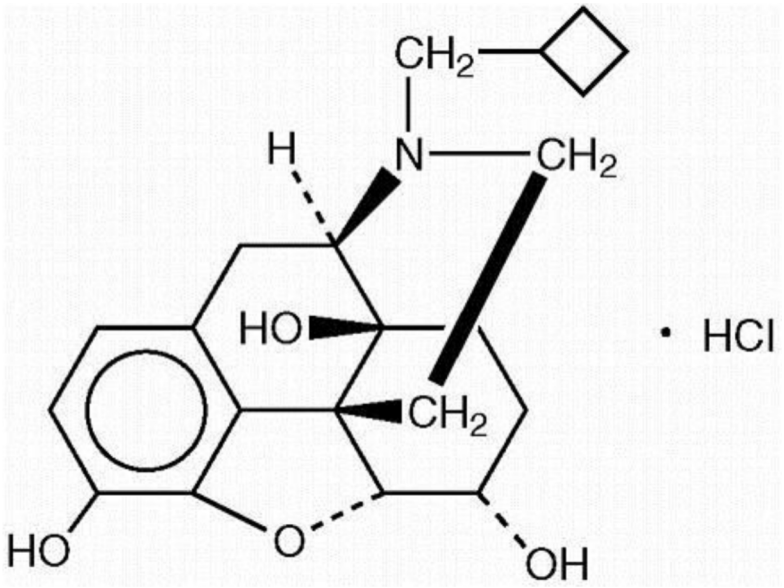

Fig.11.chemical structure of nalbuphine

CHEMICAL NAME

17 - (cyclobutylmethyl) - 4, 5 - epoxy, morphinan-3, 6,1 4 - triol, hydrochloride

RECEPTOR INTERACTION

Nalbuphine hydrochloride binds to mu(μ), kappa(κ), and delta(δ) receptors, but not to sigma receptors. Nalbuphine hydrochloride is primarily a κ agonist/μ antagonist analgesic. Nalbuphine hydrochloride has an analgesic potency[26] similar to that of morphine. The narcotic antagonist activity of nalbuphine hydrochloride is nearly one-fourth(1/4th) as potent as that of nalorphine and it is ten times potent as that of pentazocine. When nalbuphine administered subsequent or concurrent with μ agonist opioid analgesics (e.g., morphine, fentanyl), it may partially

reverse or block opioid-induced respiratory depression from the μ agonist analgesic.

MECHANISM OF ACTION

By its agonist action, nalbuphine hydrochloride stimulates κ receptors & thereby it inhibits the release of neurotransmitters like substance P that mediate pain. Nalbuphine acts as a post-synaptic inhibitor on the "inter neurons & output neurons" of the Spino-thalamic tract which transports nociceptive information.

PHARMACEUTICAL INFORMATION

Molecular formula - C21 H27 NO 4 .HCl

Molecular Mass - 393.91 g/mol

pKa - 8.71

PHARMACOKINETICS

Nalbuphine hydrochloride is inactive orally and intravenous route is the conventional route of administration. Nalbuphine can also be administered by intramuscular, subcutaneous, neuraxial routes. Bio-availability is around 80%. Volume of distribution(Vd) is 3.8litres/kg. Onset of action Intravenous administration is within 2-3 mins & by subcutaneous, intramuscular it is < 15 mins

Plasma half life - 5 hrs. Duration of analgesia - 3 to 6 hrs. Nalbuphine hydrochloride is primarily metabolized in the liver and the metabolites are

excreted via kidney. The dosage of nalbuphine must be decreased in patients with hepatic and renal failure.

USES OF NALBUPHINE

- Used as an adjuvant to general anesthesia
- Used as an adjuvant to neuraxial anesthesia
- Used for Obstetric analgesia during labor and delivery
- Used as an adjuvant to peripheral nerve blocks.
- Used in the management of postoperative pain.

ALSO USED FOR:

- Opioid induced pruritus and respiratory depression[27]
- Shivering
- Sickle cell anemia with crisis

PREPARATIONS AND STORAGE

- It is available as 10mg, 20mg solutions in 1ml ampoule.
- It should be stored at room temperature (15°c to 30°c).
- To be protected from excessive light.

Fig.12.Ampoule of nalbuphine

ADVERSE EFFECTS

The most common side effects of nalbuphine hydrochloride are sedation, sweating, nausea, vomiting, dizziness, vertigo, dry mouth, headache. Other side effects are bradycardia, hypotension, urinary urgency. Because of the ceiling effect,[28] nalbuphine hydrochloride causes less respiratory depression compared to other opioids.

REVIEW OF LITERATURE

Literature related to intrathecal adjuvants added to local anaesthetics was searched in google, pubmed, medknow and metascape search engines using keywords like intrathecal nalbuphine, intrathecal fentanyl, intrathecal adjuvants added to bupivacaine , from articles 2000 to till date.

1. Mukherjee A, Pal A, Agrawal J[29] et al conducted a study in 2011 titled "Intrathecal nalbuphine as an adjuvant to subarachnoid block: What is the most effective dose?". It was a randomized, prospective double blind controlled study. Patients of ASA physical status I and II posted for elective lower limb orthopedic surgery under spinal anaesthesia were included in the study. They allotted into 4 groups A,B,C and D by computer generated randomisation.

   12.5mg -0.5% hyperbaric bupivacaine added to 0.2,0.4,0.8mg of nalbuphine and normal saline respectively according to the group allotted.

They compared the onset of sensory blockade and motor blockade and the duration of sensory blockade and motor blockade between the groups. They used Bromage scale for assessing motor block and visual analogue scale for assessing pain. The onset time of sensory blockade and motor blockade was significantly ($p<0.05$) reduced and the

duration of block was prolonged in nalbuphine groups. They observed that when nalbuphine was added as an adjuvant the analgesic effect of bupivacaine was significantly prolonged. The authors observed and concluded that 0.4mg nalbuphine is the most effective intrathecal dose that increases the duration postoperative analgesia with no side-effects.

2. Jyothi B, Shruthi Gowda, Safiya Shaikh[30] did a study in 2014 titled "A comparison of analgesic effect of different doses of intrathecal nalbuphine hydrochloride with bupivacaine and bupivacaine alone for lower abdominal and orthopedic surgeries". Hundred patients of both sexes under ASA I and II were included in the study. They were randomly allocated into 4 groups I, II, III, IV. Study was a double blind randomized controlled study. Prior to Subarachnoid block, monitors like ECG, pulse oximetry (pulse rate,Spo2), non invasive blood pressure (NIBP) were connected. Base line values were recorded. Under SAB, 15mg bupivacaine + 0.5ml of NS(Group I) or 15mg of bupivacaine with any of nalbuphine dosage 0.8mg, 1.6 and 2.5mg (Group II,III and IV) was given. The two segment regression time of sensory blockade was increased and duration of analgesia was significantly prolonged in nalbuphine groups. The postoperative pain scores were drastically reduced in group II ,III & IV than group I (3.4±0.4 vs 4.08±0.5). Finally they concluded that addition of 0.8mg nalbuphine to 0.5% hyperbaric

bupivacaine intrathecally provides excellent and prolonged analgesia. No significant side effects.Analgesic ceiling effect noted at 0.8mg dosage, and further increase in dose didn't rise the analgesic efficacy.

3. Shehla shakooh, Pooja Bhosle[31] conducted a study in 2004 titled "Intrathecal nalbuphine; An effective adjuvant for post operative analgesia". It was a prospective randomized double blind study. 60 patients under ASA Physical Status I and II posted for elective lower abdominal surgery and lower limb surgery were enrolled in the study. Patients were divided into 2 groups by slips in the box technique. Group N received 0.5% heavy bupivacaine (3cc) + 0.8mg nalbuphine, Group B received 0.5% heavy bupivacaine (3cc). Hemodynamic parameters HR, spo2,NIBP were observed throughout the procedure. Sensory block and motor block were assessed by pinprick and Bromage scale respectively. The authors concluded that the onset of sensory blockade and motor blockade were earlier in group N with a significant p value (0.001). The duration of sensory blockade & motor blockade and the postoperative analgesia duration were superior in group N (nalbuphine group) as compared to group B. No significant side effects were reported between the two groups.

4. Mostafa Galal, Mohamad F[32] et al did a study in 2011 regarding "Which has greater analgesic effect: Intrathecal Nalbuphine or Intrathecal Tramadol?". 60 patients posted for Transurethral resection of the bladder tumor (TURBT) under the ASA PS I and II were included in the study. They were randomly divided into 2 groups.Received 15mg of 0.5% hyperbaric bupivacaine + 50mg of tramadol hydrochloride preservative free/2mg of nalbuphine hydrochloride preservative free according to the group allotted..

Subarachnoid block was performed with 25G Quincke's needle in L3-L4 space with Patient in right lateral decubitus position. They studied postoperative analgesic requirements, sedation scores & Visual Analog Scale (VAS) for pain intensity and side effects.

The authors finally concluded that intrathecal tramadol and intrathecal nalbuphine when used with bupivacaine 0.5% produce similar postoperative analgesia, however the sedation scores were higher in tramadol group.

5. Ravikiran J Thote, Prashant Lomate, Shilpa Gaikwad[33] et al conducted a study in 2015 titled " Comparison among intrathecal fentanyl and nalbuphine hydrochloride in combination with bupivacaine and plain bupivacaine for lower limb surgeries". It was a prospective randomized controlled double blind study. 60 patients of both sexes posted for lower limb surgeries under ASA Physical

status I and II were included in the study. They were segregated into three groups of twenty patients each using computer generated random numbers. They compared 25mcg of fentanyl and 500mcg of nalbuphine added to 2.5ml of 0.5% hyperbaric bupivacaine and with Group III - received 2.5ml of 0.5% hyperbaric bupivacaine + 0.5ml of normal saline.

They finally concluded that the onset of sensory blockade and motor blockade were significantly earlier in fentanyl and nalbuphine group. However the duration of sensory blockade was prolonged with nalbuphine bupivacaine combination than fentanyl bupivacaine combination. Sedation at the level of arosoubility without any respiratory depression was noted with nalbuphine.

6. Bindra TK, kumar P et al[34] conducted a study in 2018 titled "postoperative analgesia with Intrathecal Nalbuphine versus Intrathecal Fentanyl in cesarean section:" A Double –blind Randomized comparative study.

In this study 150 parturients of ASA PS I and II of age group 20-45yrs with normal coagulation profile undergoing cesarean section under spinal anaesthesia were enrolled. These Patients were randomized into three groups. Group I,II,III & each group of fifty patients. They received 2ml

bupivacaine + 0.4ml nalbuphine (groupI) /0.4ml fentanyl(group II)/0.4ml normal saline (group III)respectively.

They finally concluded both intrathecal nalbuphine 0.8mg and fentanyl 20μg are effective adjuvants to 0.5% heavy bupivacaine.They also concluded that the duration of analgesia is maximally prolonged by nalbuphine when compared to fentanyl and hence nalbuphine may be used as an alternative to fentanyl in cesarean section.

7. Chatrath V, Attri[35] et al performed a study in 2015 regarding "The effect of epidural nalbuphine for postoperative analgesia in orthopedic surgery". A study was performed with 80 adult patients of (ASA) PS I and II category posted for elective lower limb orthopedic surgeries under combined spinal & epidural anaesthesia. Patients were divided into two categories using computer randomization method. Patients received epidurally 10ml of 0.25% bupivacaine + 10mg nalbuphine or 100mg tramadol.

Subarachnoid block (SAB) was given with 0.5% of 2.5ml bupivacaine in both the groups. Epidural top up was given at sensory regression to T10. Mean duration of analgesia & mean sedation score were compared between the two groups. They finally concluded that the quality of analgesia and patient satisfaction score were better with nalbuphine epidurally than with epidural tramadol.

8. Hala Mostafa Gomaa, Nashwa nabil Mohamed[36] et al did a study in 2013 titled "A comparison between post-operative analgesia after intrathecal nalbuphine with bupivacaine, and intrathecal fentanyl with bupivacaine after cesarean section". 60 pregnant females posted for elective LSCS under the ASA PS II were included in the study. The patients after obtaining informed consent were divided into 2 groups. Patients received 0.5% hyperbaric bupivacaine + 0.5ml fentanyl(25μg) intrathecally or 0.5ml nalbuphine hydrochloride(0.8mg) intrathecally according to the group allotted.. They finally concluded that time for to reach the T10 sensory segment was not significantly different between the two groups (F&N). However, the duration of intraoperative analgesia & postoperative analgesia was prolonged in group N compared to group F.
9. Pallavi Ahluwalia, Amit Ahluwalia[37] et al performed a study in 2015 titled "A prospective randomized double-blind study to evaluate the effects of intrathecal nalbuphine, in patients of lower abdominal surgeries under spinal anaesthesia". They conducted study in 70 adult patients posted for lower abdominal surgeries who were enrolled in the study. They were randomly divided into two groups (GroupN&Group C). Group N received 2.5ml of 0.5% hyperbaric bupivacaine + nalbuphine 0.8mg (made upto 0.5ml)

intrathecally. Group C received 2.5ml of 0.5% hyperbaric bupivacaine + normal saline (0.5ml) intrathecally. They concluded that the addition of nalbuphine as adjuvant to bupivacaine intrathecally fastens the the time of onset of sensory blockade (1.29±0.43min vs 3.78±1.31min) and prolongs the duration of sensory blockade and motor blockade. The time to first analgesic requirement was prolonged in group N (nalbuphine group) as compared to group C (298.43±30.92min vs 201.31±34.31min).

10. Xavier Culebras, Giovanni Gaggero[38] et al did a study in 2000 titled "Advantages of Intrathecal Nalbuphine, Compared with Intrathecal Morphine, After Cesarean Delivery: An Evaluation of Postoperative Analgesia and Adverse Effects". After the approval from ethical committee and getting informed consent, 90 healthy parturients at term for elective cesarean delivery under spinal anaesthesia were enrolled in the study. It was a randomized, prospective double blinded study. Patients received 10mg of 0.5% hyperbaric bupivacaine with either morphine 0.2mg (category A), nalbuphine 0.2mg (category B), nalbuphine 0.8mg (category c) & nalbuphine 1.6mg (categoryD).

They found that postoperative analgesia was significantly prolonged in the morphine category than nalbuphine ($P < 0.0001$). Among the nalbuphine categories, postoperative analgesia was prolonged with

0.8mg (category c). Adverse effects like pruritus, nausea and vomiting were more with morphine when compared to nalbuphine. APGAR scores were similar in all groups. There was no newborn or maternal respiratory depression with both groups. The authors had finally concluded that 0.8mg intrathecal nalbuphine provides good intraoperative analgesia and improves postoperative analgesia without adverse effects.

11. Gurunath BB et al[39]., conducted a study in 2018 titled "Postoperative analgesic efficacy of intrathecal fentanyl, compared to nalbuphine with bupivacaine in spinal anaesthesia for lower abdominal surgeries". In this study 124 patients aged 18-55yrs under ASA PS I and II were randomized into 2 groups, Group N and Group C and they received nalbuphine (300µg) + hyperbaric bupivacaine & fentanyl (25 µg) + hyperbaric bupivacaine respectively. They concluded that Group N nalbuphine 300µg with 3ml of0.5% hyperbaric bupivacaine had increased in onset time of sensory blockade and had increased duration of postoperative analgesia, increased duration of sensory blockade and minimal bradycardia that could be managed easily.

12. Moustafa AA, Baaror AS, Abdelazim IA[40] et al did a study titled "Comparative study between nalbuphine and ondansetron in prevention of intrathecal morphine -induced pruritus in women undergoing cesarean section". 90 pregnant women of ASA PS II

scheduled for cesarean delivery under spinal anaesthesia (SAB) were recruited for this study. They were divided into three groups. SAB performed in left lateral position at L3-4 interspace using 25G Quincke spinal needle with 2.2ml of 0.5% hyperbaric bupivacaine and 0.2mg morphine. Immediately after delivery of baby they received one of the following

- Placebo group (P) - received 4ml of normal saline(NS) IV injection.
- Nalbuphine group (N) - received 4ml of 4mg nalbuphine IV.
- Ondansetron group (O) - received 4ml of 4mg ondansetron IV.

Patients were observed for pruritus scores, blood pressure, heart rate and SPO2 in the post anaesthesia care unit (PACU) for 4 hours. Both nalbuphine and ondansetron were effective for prevention of intrathecal morphine induced pruritus in parturients undergoing cesarean delivery. However among nalbuphine & ondansetron, nalbuphine was preferred because it is not excreted in breast milk.

13. Rajni Gupta et al[41] (2011) with an aim to evaluate the onset and duration of sensory block and motor block, hemodynamic effect, postoperative analgesia, and adverse effects of dexmedetomidine or fentanyl given intrathecally as adjuvant with 0.5% hyperbaric bupivacaine conducted a study in 60 patients classified in ASA PS I and II scheduled for lower abdominal surgeries. Patients were randomly alloted to receive either 12.5 mg hyperbaric bupivacaine +

5μcg dexmedetomidine (group D, n=30) or 12.5 mg hyperbaric bupivacaine + 25 μcg fentanyl (group F, n=30) intrathecal. The mean time of sensory regression to reach S1 level was 476±23 min in group D and 187±12 min in group F(P<0.001). The regression time of motor block to reach modified Bromage score 0 was 421±21 min in group D and 149±18 minutes in group F (P<0.001). They finally concluded that intrathecal dexmedetomidine was associated with prolonged motor block and sensory block, hemodynamic stability, and reduced demand for rescue analgesics in 24 hrs when compared to fentanyl.

14. Hem Anand Nayagam et al [(42)](2014) did a prospective randomized double blind study of intrathecal fentanyl & dexmedetomidine added to low dose bupivacaine for spinal anaesthesia for lower abdominal surgeries in one hundred & fifty patients. Group F (*n* = 75) received bupivacaine 0.5% hyperbaric (0.8 ml) + fentanyl 25 μcg (0.5 ml) + normal saline 0.3 ml and Group D (*n* = 75) received bupivacaine 0.5% hyperbaric (0.8 ml) + dexmedetomidine 5μcg (0.05 ml) + normal saline 0.75 ml, aiming for a final concentration of 0.25% of bupivacaine (1.6 ml), administered intrathecally. Time taken to reach T10 block level, peak sensory block level (PSBL), time taken to reach peak block level, time taken to two segment regression (TTSR), the degree of motor block (MBS), side-effects and the time

to first analgesic request (TFAR) were recorded. PSBL (P = 0.000) and TFAR (P = 0.000) were highly significant. Mean time to PSBL (<0.05) and MBS (P = 0.035) were significant. They finally concluded that the clinical advantage of dexmedetomidine over fentanyl. Dexmedetomidine facilitated the spread of the block and offered prolonged post operative analgesia compared to fentanyl.

AIM OF THE STUDY

The aim of the study was to Compare intrathecal nalbuphine vs fentanyl added to 0.5% hyperbaric bupivacaine for perioperative anaesthesia and postoperative analgesia in patients undergoing hernioplasty.

OBJECTIVES

Objective of the study was to compare the

Outcome measures:

Primary measure:

Sensory block onset time (sensory level T10)

Motor block onset time(Bromage 3)

Highest level of sensory block reached and time taken to reach it.

Time taken for two segment regression of sensory level

Duration of motor block

Duration of analgesia

Secondary measure:

Haemodynamic parameters

Side effects

MATERIALS AND METHODS

This study was done in Tirunelveli medical college hospital,at Department of Anaesthesiology and critical care from December 2017 to September 2018.

STUDY DESIGN

It was a Single centre, prospective, randomized double blinded, interventional controlled study.

After obtaining institutional ethical committee approval, 120 patients posted for elective hernioplasty surgery under spinal anaesthesia with satisfying inclusion criteria were enrolled in the study after obtaining informed consent from the patients and relatives.

RANDOMIZATION :

3 Groups by random number allotted by slips in the box technique

ALLOCATION & INTERVENTION: 3 Groups

n = 40

Group A : 15mg (3 ml) of 0.5% hyperbaric bupivacaine and nalbuphine 0.5 mg (0.5ml) - Total volume 3.5 ml.

Group B received 15mg (3 ml) of 0.5% hyperbaric bupivacaine and fentanyl 0.25 mcg (0.5ml) - Total volume 3.5 ml.

Group C received 15mg (3 ml) of 0.5% hyperbaric bupivacaine and normal saline 0.5 ml (0.5ml)- Total volume 3.5ml

INCLUSION CRITERIA

- 20 - 60 years of age
- ASA physical status I or II
- Patients who gave valid informed written consent
- Patients undergoing elective hernioplasty.

EXCLUSION CRITERIA

- Patients having any absolute contraindications for spinal anaesthesia
- Infection at the subarachnoid block injection site
- Patients with neurological and musculoskeletal disease
- Patients with bleeding disorders
- Patients on anticoagulants
- History of allergy to local anaesthetics and Obese patients (obesity BMI > 30kg/m^2).

PRE-OPERATIVE ASSESSMENT

All the patients were duly examined on the day prior to surgery and pre-operative assessment sheet was checked. The height (cms), weight(kg), body mass index(BMI), of the patient were measured. The airway assessment, spine examination and the nutritional status of the patient were evaluated. A detailed general and systemic examination was done. Preoperative investigations like complete haemogram (CBC), renal function tests(RFT), random blood sugar, blood grouping and typing,

coagulation profile, electrocardiography and chest X ray were evaluated properly.

PREMEDICATION

All the patients were fasted overnight. They were pre-medicated with tablet ranitidine 150mg, tablet metoclopramide 10mg, and tablet alprazolam 0.5mg on the night before surgery.

PREPARATION

Upon arrival to the operating room, standard monitors like non invasive blood pressure(NIBP), Electrocardiography(ECG) and pulse oximetry(SPO2) were connected and baseline values were recorded. An intravenous line was secured with 18G cannula. After securing iv line, patients were preloaded with10ml/kg of Ringer Lactate (RL) solution.

TECHNIQUE:

The patient was placed in the right lateral decubitus position. Under strict aseptic precautions, lumbar puncture was performed at L3-L4 intervertebral space using 25 G quincke's needle using the midline approach. After confirming free flow of clear cerebrospinal fluid(CSF), drug was injected at 0.2ml/sec, according to the groups allocated as described above.

Oxygen at 4l/min was administered through face mask. Hemodynamic parameters like peripheral oxygen saturation(spo2), non

invasive blood pressure(NIBP), pulse rate were recorded at regular intervals intraoperatively and postoperatively.

MONITORING

- Hypotension was defined as systolic blood pressure less than 90mm Hg or less than 20% from baseline, which was treated with Inj. Ephedrine 6mg iv bolus.
- Bradycardia was defined as heart rate less than 60 beats/min, which was treated with - Inj. Atropine 0.6 mg iv bolus.

Sensory block was assessed by pinprick method in the mid-clavicular line using 27G needle, every minute until the block reached T6 dermatome. After that, level was checked every 2 mins until maximal sensory block was attained.

GRADES OF SENSORY BLOCKADE

GRADE 0 - Sharp pain is felt

GRADE 1 - Analgesia, dull sensation is felt

GRADE 2 - Anesthesia, no sensation is felt

Onset of sensory blockade was defined as the time interval between the end of anesthetic injection to loss of sensation to pinprick at T10 level.

MOTOR BLOCKADE

The quality of motor block was assessed by modified Bromage scale.

GRADE 0 - no motor blockade, patient able to lift the leg at the hip.

GRADE 1 – patient able to flex the knee and ankle but not able to lift the

leg at the hip (hip blocked)

GRADE 2 -patient able to move the foot only (hip and knee blocked)

GRADE 3 –patient unable to move even the foot (hip, knee and ankle blocked).

Onset of complete motor blockade was defined as the time interval taken between the completion of study drug injection until Bromage 3 was registered.

Surgery was started after complete anaesthesia was attained. At the end of the surgery, both sensory and motor level were noted. Time taken for two segment regression from the maximal level was noted. Postoperatively, patients were regularly followed up and monitored in the recovery and postoperative ward.

VISUAL ANALOG SCALE

Before surgery patients were explained about Visual Analog Scale(VAS) . The scores were periodically evaluated in the postoperative ward and rescue analgesia was given at a VAS score of 4 or more.

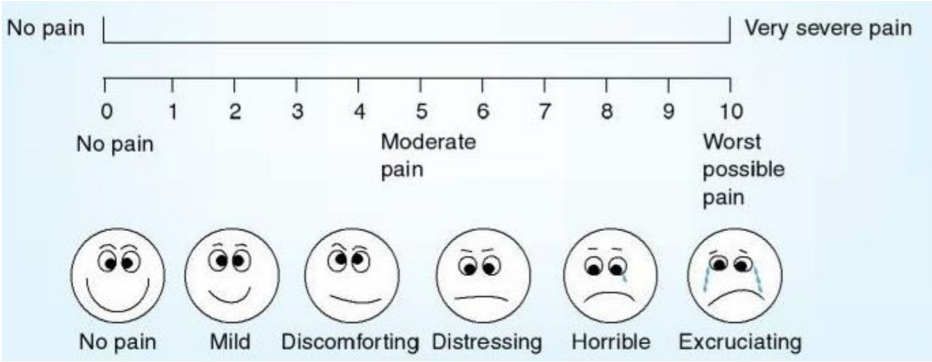

Fig.14. VISUAL ANALOG SCALE

0-10 VAS Numeric Pain Distress Scale

SCORE 0-2 =NO PAIN

SCORE 2-4= MILD PAIN

SCORE 4-6= MODERATE PAIN

SCORE 6-8 =SEVERE PAIN

SCORE 8-10 =UNBEARABLE PAIN

STATISTICS AND RESULTS

Statistical Analysis:

Data were analysed with SPSS version 16 and Microsoft excel. Comparison of three groups were done by using one way Anova. Descriptive results were calculated using mean and standard deviation. An P value of less than 0.05 was considered statistically significant. Sample size was calculated using the formula $n=(u+v)2 \times(SD1^2+SD2^2)\div(\mu1-\mu2)$with atleast 90 sample size needed to detect a difference with more than 80% power of study at 5% significance level.

OBSERVATION AND ANALYSIS

All 120 patients with ASA physical status I/II who satisfied all inclusion criteria were randomly divided into three groups and underwent Hernioplasty under subarachnoid block in Tirunelveli medical college Hospital, attached to Tirunelveli Medical College, Tirunelveli. All the patients completed the study without any exclusion.

The collected data were analyzed by one-way ANOVA and results obtained in form of mean and standard deviation. The probability value $p < 0.05$ is considered as statistically significant. comparison of the resuts :

DEMOGRAPHIC DATA

Demographically all patients were comparable with regards to age, height and weight.

Age distribution

Mean age in three groups were around 44 . The p value for mean age was not stastitically significant (p value = 0.418).

Age distribution

AGE	No of Patients	Mean (Years)	Std. Deviation	P value
Group A	40	44.13	10.84	0.418
Group B	40	45.83	9.22	
Group C	40	42.58	12.60	
Total	120	44.18	10.96	

Tab 1: Age distribution

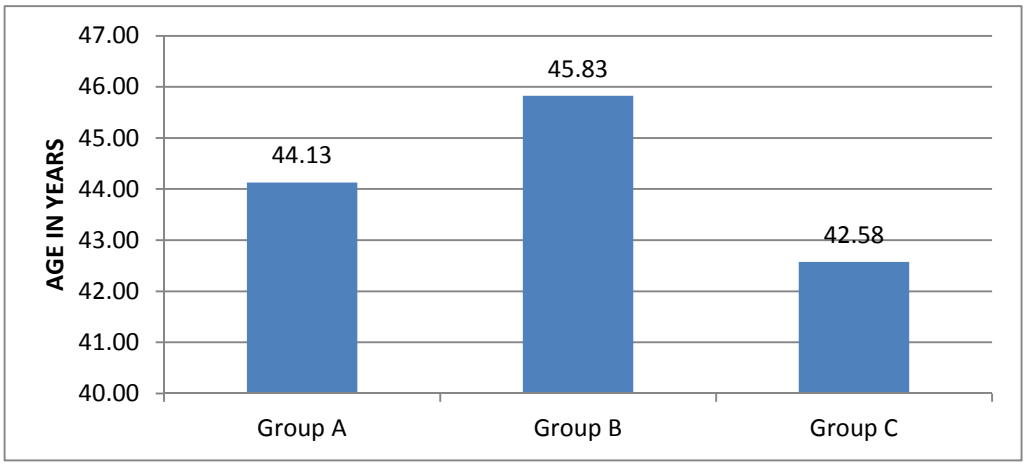

Chart 1: Age Distribution

Height Distribution:

Mean height was not statistically significant, (p value=0.202).

Height	No of Patients	Mean (CM)	Std. Deviation	P value
Group A	40	165.08	3.54	0.202
Group B	40	165.28	3.40	
Group C	40	163.98	3.49	
Total	120	164.78	3.50	

Tab.2. Height distribution(height in cms)

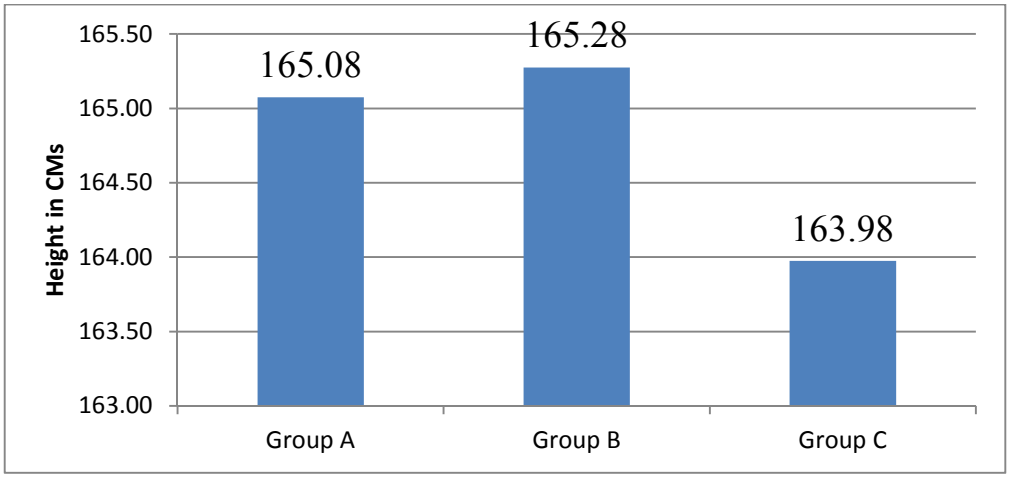

Chart 2: HEIGHT DISTRIBUTION

WEIGHT DISTRIBUTION

Mean weight was not statistically significant, (p value=0.652).

Weight	No of Patients	Mean (Kg)	Std. Deviation	P value
Group A	40	63.98	5.06	
Group B	40	64.90	3.77	
Group C	40	64.53	3.92	0.652
Total	120	65.13	4.44	

Table .3 Weight Distribution

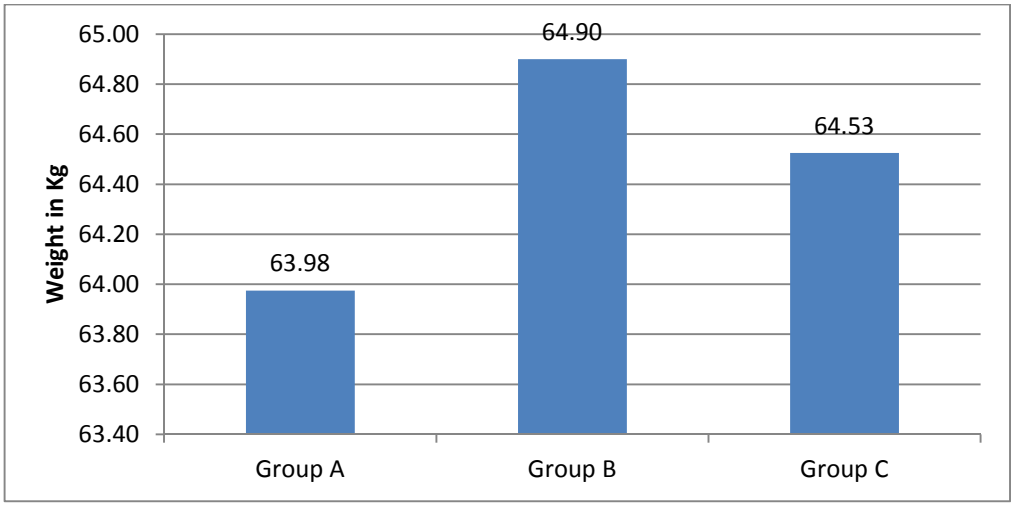

Chart 3: Weight distribution

GROUP A - BUPIVACAINE + NALBUPHINE

GROUP B - BUPIVACAINE + FENTANY

GROUP C - BUPIVACAINE + NORMAL SALINE

ASA status comparison

GROUP	ASA		Total	P value
	I	II		
Group A	16	24	40	0.529
Group B	21	19	40	
Group C	19	21	40	
Total	56	64	120	

Table.4 ASA status comparison

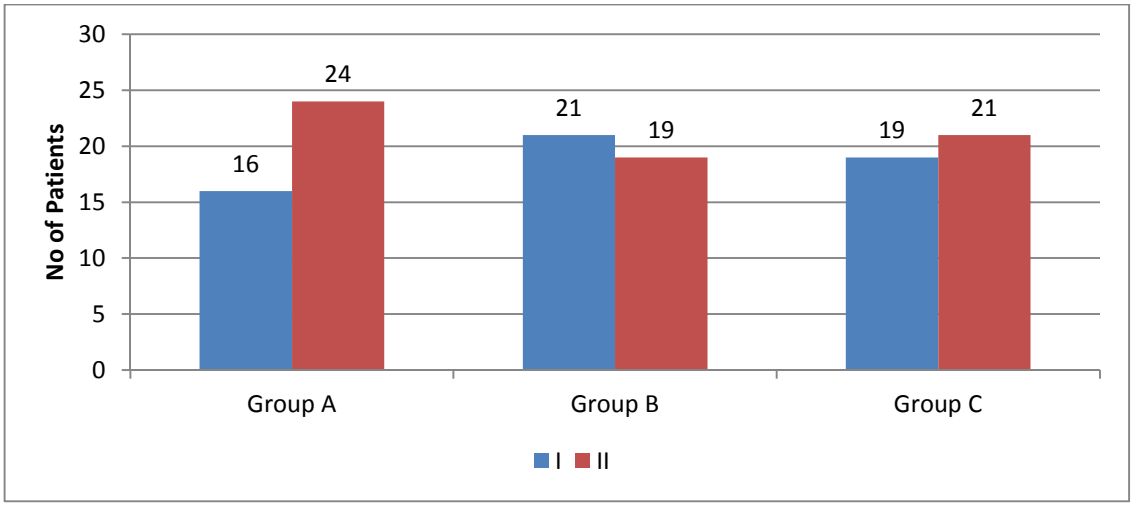

Chart 4: ASA status

GROUP A - BUPIVACAINE + NALBUPHINE

GROUP B - BUPIVACAINE + FENTANYL

GROUP C - BUPIVACAINE + NORMAL SALINE

ASA - American Society of Anesthesiologist

Sensory block onset time comparison:

SOT	N	Mean	Std. Deviation	P value
Group A	40	3.05	0.88	<0.0001
Group B	40	2.25	0.63	
Group C	40	4.08	1.25	
Total	120	3.13	1.21	

Table.5.SOT comparison

Dependent Variable			Mean Difference (I-J)	P value
SOT	Group A	Group B	0.80	0.001
		Group C	-1.03	0.000
	Group B	Group A	-0.80	0.001
		Group C	-1.83	0.000
	Group C	Group A	1.03	0.000
		Group B	1.83	0.000

Table.6. SOT multiple comparison

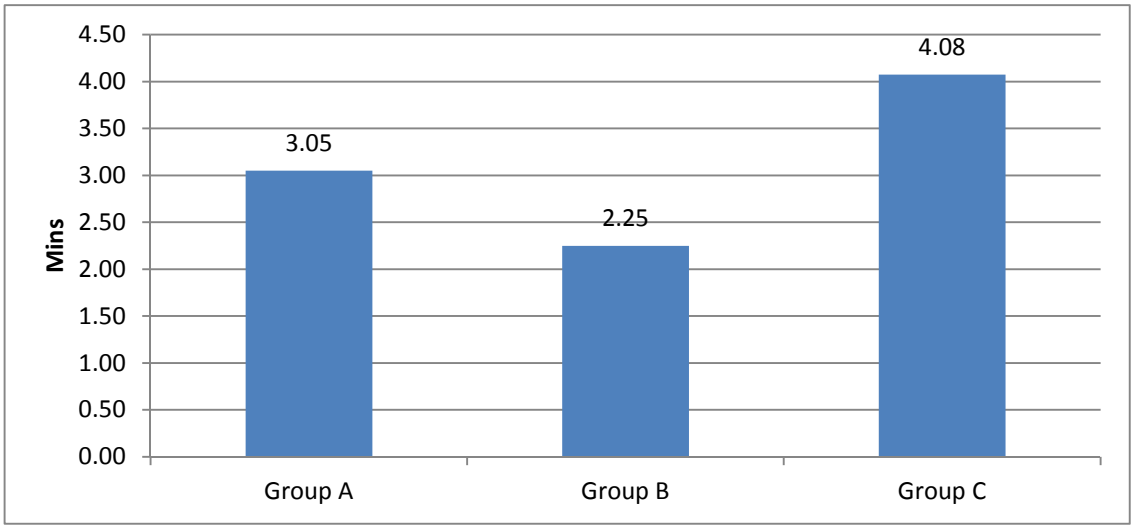

Chart 5: SOT comparison

Comparison of mean time of onset of sensory block is statistically significant among three Groups (P value <0.0001) . Sensory block onset time of Group B is much earlier than Group A and it is statistically significant (P value 0.001). Sensory block onset time of Group A is much earlier than Group C and it is statistically significant (P value 0.000).

Comparison of Time to reach highest level of sensory block:

THSL	N	Mean	Std. Deviation	P value
Group A	40	13.75	2.06	
Group B	40	11.68	2.44	
Group C	40	14.54	3.54	
Total	120	12.92	2.87	0.002

Table.7.THSL comparison

Dependent Variable			Mean Difference (I-J)	P value
THSL	Group A	Group B	2.08	0.003
		Group C	-0.79	0.125
	Group B	Group A	-2.08	0.003
		Group C	-2.82	<0.0001
	Group C	Group A	0.79	0.125
		Group B	2.82	<0.0001

Table.8.THSL multiple comparison

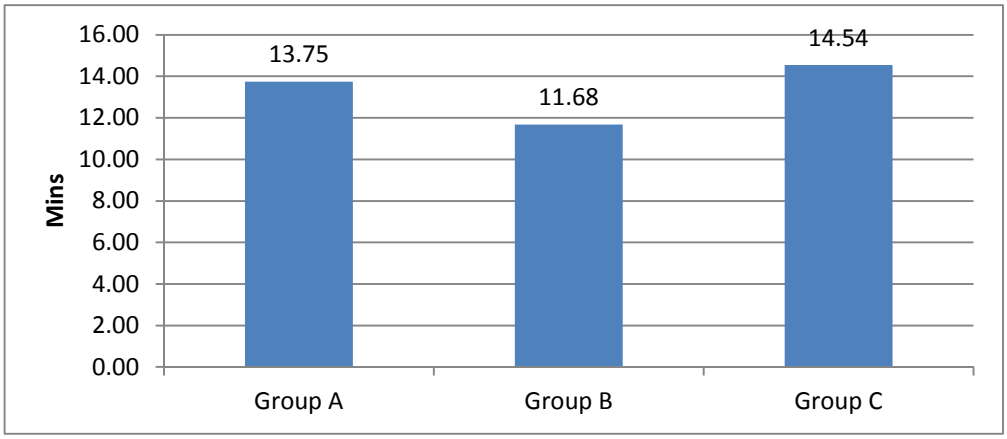

Chart 6: THSL comparison

Comparison of mean time to reach highest sensory level among three Groups is statistically significant (P value0.002). Time to reach highest sensory level of Group B is much earlier than Group A and it is statistically significant (P value 0.003). Time to reach highest sensory level of Group A is earlier than Group C and it is not statistically significant.

Comparison of mean time for two segment regression of sensory level among three Groups:

		N	Mean	Std. Deviation	P value
TRSL	Group A	40	90.40	13.79	
	Group B	40	81.35	6.77	
	Group C	40	50.98	3.58	
	Total	120	74.24	19.19	<0.0001

Tab.9.TRSL comparison

Dependent Variable				Mean Difference (I-J)	P value
TRSL	Group A	Group B	9.05	0.000	
		Group C	39.43	0.000	
	Group B	Group A	-9.05	0.000	
		Group C	30.38	0.000	
	Group C	Group A	-39.43	0.000	
		Group B	-30.38	0.000	

Tab.10.TRSL multiple comparison

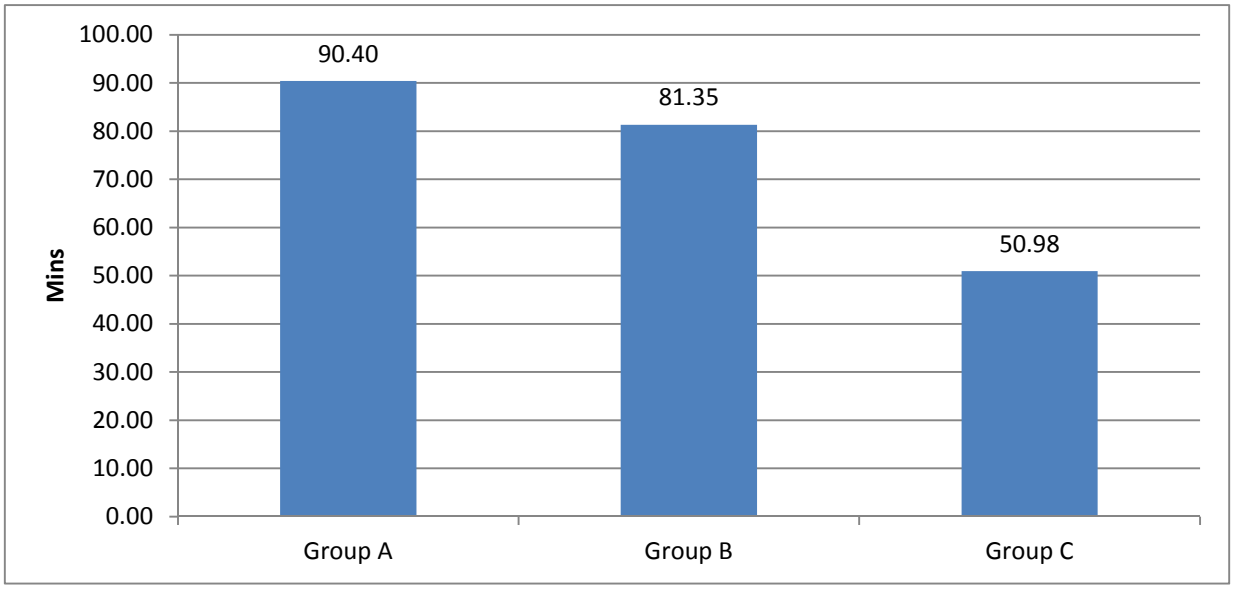

Chart 7: TRSL comparison

Comparison of mean time for two segment regression of sensory level among three groups is statistically significant (P value <0.0001). Mean time for two segment regression of sensory level of Group A is much higher than Group B and it is statistically significant (P value 0.000). Mean time for two segment regression of sensory level of Group B is higher than Group C and it is statistically significant (P value 0.000).

Comparison of mean time of onset of motor block

		N	Mean	Std. Deviation	P value
MOT	Group A	40	2.33	0.69	
	Group B	40	1.48	0.51	
	Group C	40	3.43	0.93	
	Total	120	2.41	1.08	<0.0001

Tab.11.MOT comparison

Dependent Variable			Mean Difference (I-J)	P value
MOT	Group A	Group B	0.85	0.000
		Group C	-1.10	0.000
	Group B	Group A	-0.85	0.000
		Group C	-1.95	0.000
	Group C	Group A	1.10	0.000
		Group B	1.95	0.000

Tab.12.MOT multiple comparison

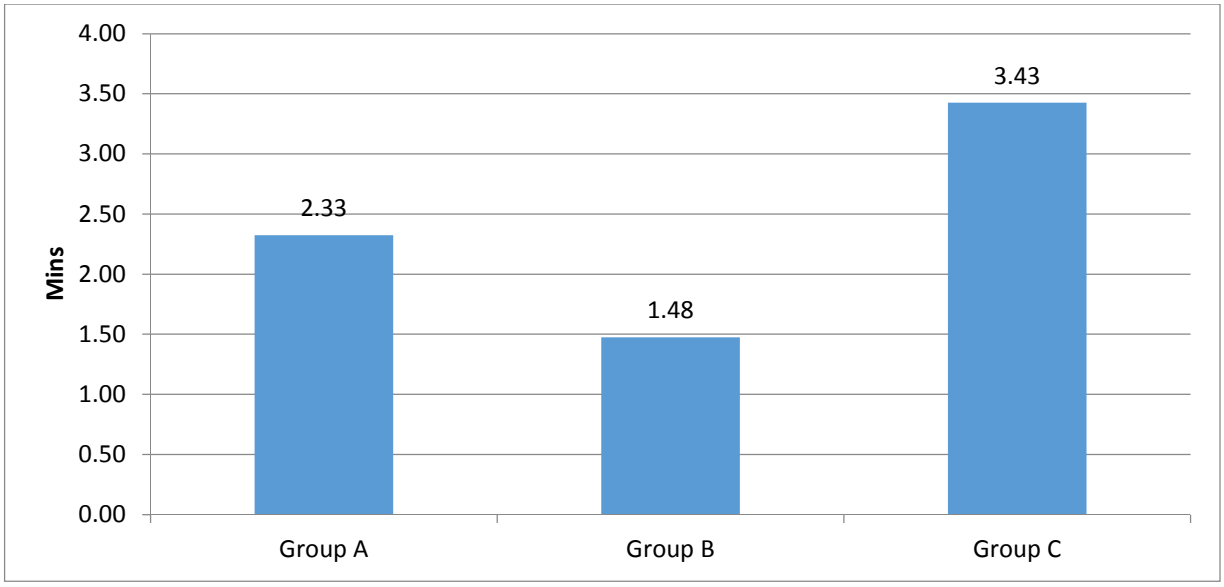

Chart 8: MOT comparison

Comparison of mean time of onset of motor block among three groups is statistically significant (P value <0.0001). Mean time for onset of motor block of Group B is earlier than Group A and it is statistically significant (P value 0.000). Mean time for onset of motor block of Group A is higher than Group C and it is statistically significant (P value 0.000).

Comparison of highest sensory level reached among three Groups:

		HSL					Total	P value
		T2	T3	T4	T5	T6		
group	Group A	14	0	22	4	0	40	<0.0001
	Group B	2	2	20	16	0	40	
	Group C	0	0	1	8	31	40	
Total		16	2	43	28	31	120	

Tab.13.HSL comparison

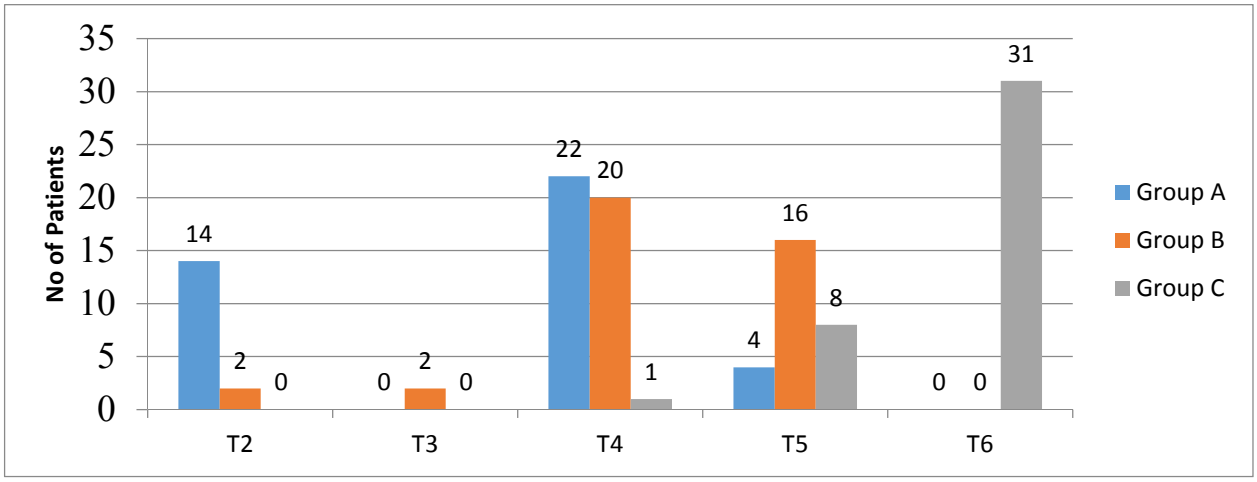

Chart 9: HSL comparison

The Median Highest sensory level reached in Group A T2 level (14 patients) and the range is from (T2 to T5). The Median Highest sensory level reached in Group B T2 level (2 patients) and the range is from (T2 to T5). The Median Highest sensory level reached in Group C T4 level (1 patient) and the range is from (T4 to T6). Comparison is statistically significant (P value <0.0001).

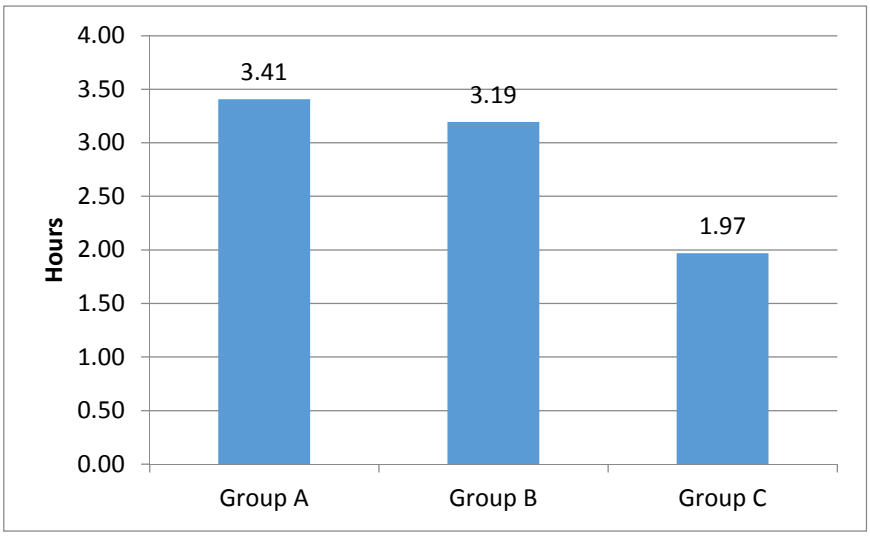

Chart 10: Comparison of duration of Motor block:

		N	Mean	Std. Deviation	P value
DMB	Group A	40	3.41	.322	<0.0001
	Group B	40	3.19	.747	
	Group C	40	1.97	.358	
	Total	120	2.86	.815	

Tab .14.DMB comparison

Dependent Variable			Mean Difference (I-J)	P value
DMB	Group A	Group B	.214	.195
		Group C	1.439*	.000
	Group B	Group A	-.214	.195
		Group C	1.225*	.000
	Group C	Group A	-1.439*	.000
		Group B	-1.225*	.000

Tab.15.DMB multiple comparison

Mean duration of motor block of Group A is(3.41 .322 hrs) higher than Group B (3.19 .747) and Group C (1.97 .358) and its statistically significant (P value 0.0001).In multiple comparison mean duration of motor block of both Group A and B are much higher than Group C and its statistically significant (P value 0.000).

Comparison of duration of analgesia:

		N	Mean	Std. Deviation	P value
DOA	Group A	40	5.15	.350	<0.0001
	Group B	40	4.05	.539	
	Group C	40	2.64	.349	
	Total	120	4.36	4.702	

Tab.16.DOA comparison

Dependent Variable			Mean Difference (I-J)	P value
DOA	Group A	Group B	1.090	.000
		Group C	2.5	.000
	Group B	Group A	-1.090	.000
		Group C	1.410	.000
	Group C	Group A	-2.5	.000
		Group B	-1.410	.000

Tab.17.DOAmultiple comparison

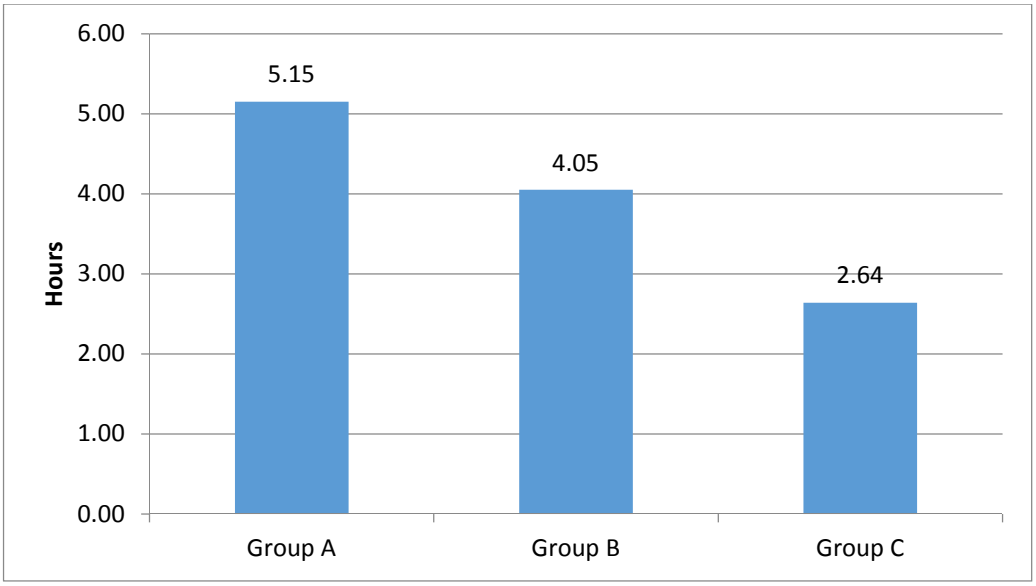

Chart 11: DOA comparison

The mean time of duration of analgesia of Group A > Group B > Group C and it is statistically significant (pvalue = < 0.0001). In multiple comparison also its statistically significant Group A vs Group B (p value 0.000), Group A vs Group C (pvalue 0.000) and Group B vs Group C (p value 0.000)

Comparison of side effects observed during study :

		complication				Total	P value
		Nil	Bradycardia	Hypotension	Shivering		
group	Group A	34	3	2	1	40	0.573
	Group B	34	4	2	0	40	
	Group C	34	2	1	3	40	
Total		102	9	4	4	120	

Tab.18 Side effects comparison

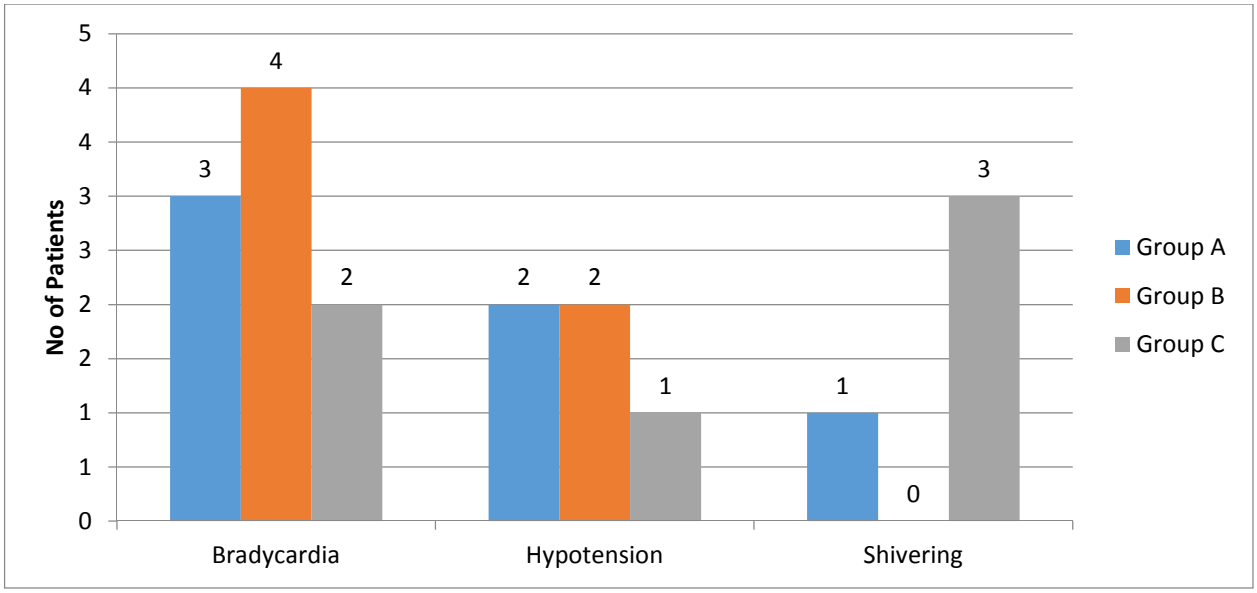

Chart 12: Side effects comparison

Side effects observed during study was very minimal and most of the cases were stable and it is not statistically significant.

Preoperative vitals

PREOPERATIVE VITALS		N	Mean	Std. Deviation	P value
SBP	Group A	40	123.90	3.62	0.327
	Group B	40	121.40	5.15	
	Group C	40	122.60	11.26	
	Total	120	122.63	7.46	
DBP	Group A	40	74.80	5.02	0.530
	Group B	40	74.15	5.50	
	Group C	40	73.55	4.26	
	Total	120	74.17	4.94	
PR	Group A	40	78.67	8.06	0.428
	Group B	40	78.80	6.50	
	Group C	40	77.70	5.76	
	Total	120	79.75	7.12	
SPO2	Group A	40	99.35	4.11	0.400
	Group B	40	99.95	0.32	
	Group C	40	100.00	0.00	
	Total	120	99.77	2.38	

Table .19. Preoperative vitals

No statistically significant difference in three groups in terms of preoperative vitals.

Comparison of systolic blood pressure among three groups: Systolic BP comparison

		N	Mean	Std. Deviation	P value
sbp0	Group A	40	118.45	4.40	
	Group B	40	115.50	5.97	
	Group C	40	117.35	3.96	
	Total	120	117.10	4.97	0.026
sbp3	Group A	40	114.50	4.72	
	Group B	40	111.30	6.97	
	Group C	40	115.50	4.29	
	Total	120	113.77	5.70	0.002
sbp6	Group A	40	109.75	6.06	
	Group B	40	108.35	6.55	
	Group C	40	112.40	5.57	
	Total	120	110.17	6.25	0.012
sbp9	Group A	40	106.03	7.08	
	Group B	40	109.25	6.62	
	Group C	40	110.00	5.91	
	Total	120	108.43	6.73	0.018
sbp12	Group A	40	108.90	7.71	
	Group B	40	110.38	6.14	
	Group C	40	109.35	6.98	
	Total	120	109.54	6.94	0.626
sbp15	Group A	40	110.80	7.23	
	Group B	40	112.20	5.41	
	Group C	40	111.55	6.83	
	Total	120	111.52	6.51	
	Total	120	68.29	4.76	0.633
sbp30	Group A	40	114.10	6.46	
	Group B	40	113.95	4.97	
	Group C	40	115.55	4.76	
	Total	120	114.53	5.45	0.353
sbp45	Group A	40	113.78	7.17	
	Group B	40	114.85	4.94	
	Group C	40	118.95	3.87	
	Total	120	115.86	5.89	
	Total	120	75.68	4.24	<0.0001

Table.20.Sbp comparison

Multiple comparrisons:

Dependent Variable			Mean Difference (I-J)	P value
sbp0	Group A	Group B	2.95	0.023
		Group C	1.10	0.939
	Group B	Group A	-2.95	0.023
		Group C	-1.85	0.273
	Group C	Group A	-1.10	0.939
		Group B	1.85	0.273

Table.21.SBP at 0min

Dependent Variable			Mean Difference (I-J)	P value
sbp3	Group A	Group B	3.20	0.030
		Group C	-1.00	1.000
	Group B	Group A	-3.20	0.030
		Group C	-4.20	0.002
	Group C	Group A	1.00	1.000
		Group B	4.20	0.002

Table.22.Sbp at 3min

Dependent Variable			Mean Difference (I-J)	P value
sbp6	Group A	Group B	1.40	0.914
		Group C	-2.65	0.160
	Group B	Group A	-1.40	0.914
		Group C	-4.05	0.010
	Group C	Group A	2.65	0.160
		Group B	4.05	0.010

Table.23.Sbp at 6min

Dependent Variable			Mean Difference (I-J)	P value
sbp9	Group A	Group B	-3.22	0.089
		Group C	-3.98	0.023
	Group B	Group A	3.22	0.089
		Group C	-0.75	1.000
	Group C	Group A	3.98	0.023
		Group B	0.75	1.000

Table.24.Sbp at 9min

Dependent Variable			Mean Difference (I-J)	P value
sbp45	Group A	Group B	-1.07	1.000
		Group C	-5.18	0.000
	Group B	Group A	1.07	1.000
		Group C	-4.10	0.003
	Group C	Group A	5.18	0.000
		Group B	4.10	0.003

Table.25.Sbp at 45min

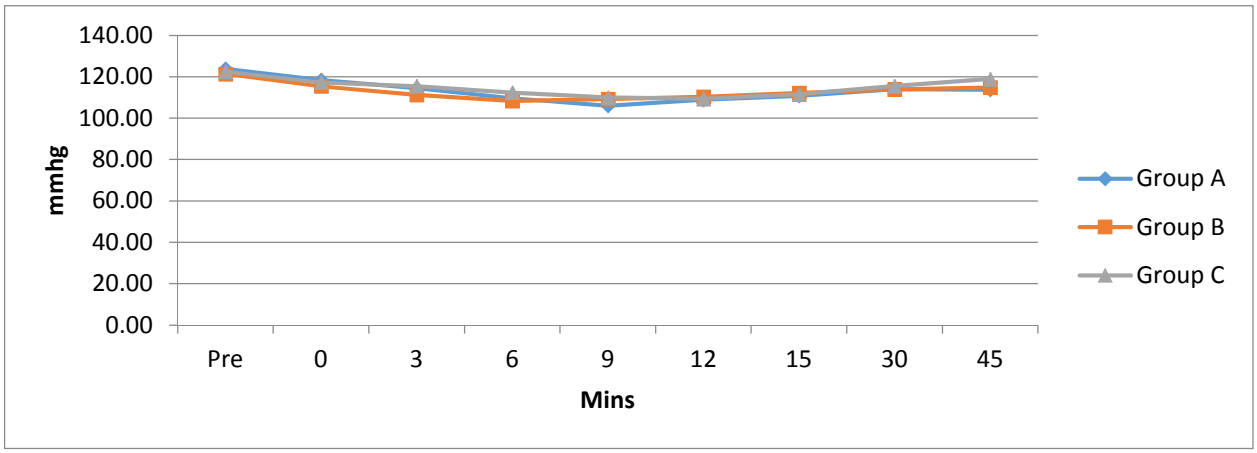

Chart: 13 Comparison of SBP

Comparison of mean systolic blood pressure among Group A, Group B, Group C is statistically significant at 0min,3min,6min,9min and 45min. In multiple comparison the mean SBP of Group A is higher than Group B & C at 0,3,6,45min. SBP of Group A is lower than Group B & C at 9min and it is statistically significant. chart 4.

Diastolic blood pressure

DBP	Group A	Group B	Group C
Pre	74.80	74.15	73.55
0.00	71.45	70.30	70.55
3.00	69.10	67.80	69.65
6.00	68.50	65.18	67.90
9.00	67.55	66.25	67.45
12.00	68.95	67.40	66.55
15.00	68.63	68.35	67.90
30.00	69.40	68.35	71.45
45.00	69.50	68.85	70.65

Tab.26.DBP

		N	Mean	Std. Deviation	P value
pre_dbp	Group A	40	74.80	5.02	
	Group B	40	74.15	5.50	
	Group C	40	73.55	4.26	
	Total	120	74.17	4.94	0.530
dbp0	Group A	40	71.45	4.10	
	Group B	40	70.30	4.31	
	Group C	40	70.55	4.57	
	Total	120	70.77	4.32	0.461
dbp3	Group A	40	69.10	3.14	
	Group B	40	67.80	5.80	
	Group C	40	69.65	4.29	
	Total	120	68.85	4.57	0.178
dbp6	Group A	40	68.50	5.20	
	Group B	40	65.18	3.77	
	Group C	40	67.90	4.32	
	Total	120	67.19	4.66	0.003
dbp9	Group A	40	67.55	4.36	
	Group B	40	66.25	4.58	
	Group C	40	67.45	4.39	
	Total	120	67.08	4.44	0.350
dbp12	Group A	40	68.95	6.88	
	Group B	40	67.40	4.23	
	Group C	40	66.55	3.76	
	Total	120	67.63	5.20	0.111
dbp15	Group A	40	68.63	5.19	
	Group B	40	68.35	4.15	
	Group C	40	67.90	4.96	
	Total	120	68.29	4.76	0.792
dbp30	Group A	40	69.40	4.47	
	Group B	40	68.35	4.12	
	Group C	40	71.45	3.90	
	Total	120	69.73	4.33	0.004
dbp45	Group A	40	69.50	5.02	
	Group B	40	68.85	3.76	
	Group C	40	70.65	2.98	
	Total	120	69.67	4.04	0.131

Tab.27.DBP comparison

Dependent Variable			Mean Difference (I-J)	P value
dbp6	Group A	Group B	3.33	0.004
		Group C	0.60	1.000
	Group B	Group A	-3.33	0.004
		Group C	-2.73	0.022
	Group C	Group A	-0.60	1.000
		Group B	2.73	0.022

Tab .28. DBP at 6min

Dependent Variable			Mean Difference (I-J)	P value
dbp30	Group A	Group B	1.05	0.787
		Group C	-2.05	0.089
	Group B	Group A	-1.05	0.787
		Group C	-3.10	0.004
	Group C	Group A	2.05	0.089
		Group B	3.10	0.004

Tab.29.DBP at 30min

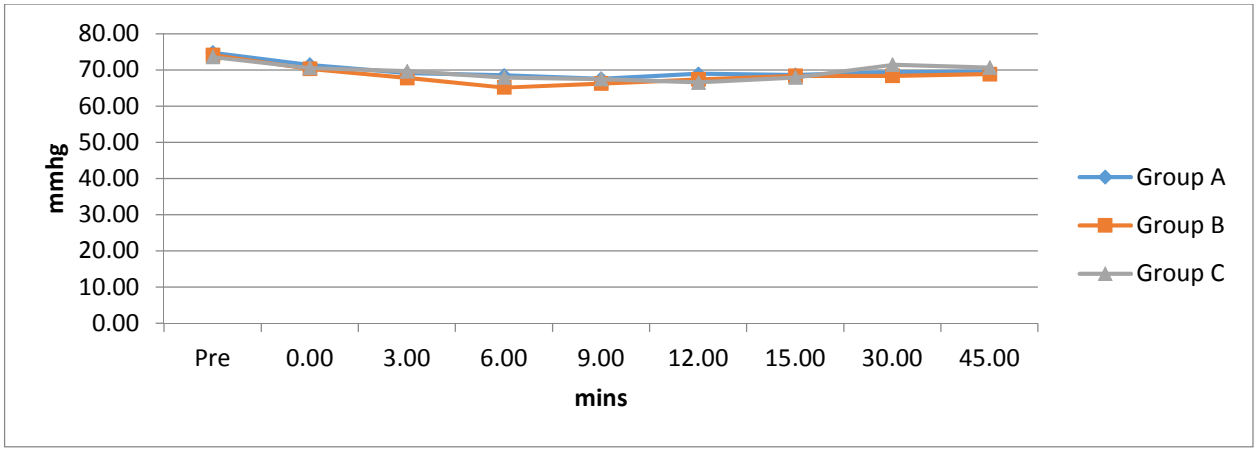

Chart: 14 DBP comparison

Comparing the mean diastolic BP of three groups is statistically significant at 6min and 30min. In multiple comparison, Mean Diastolic Bp at 6min of Group A is higher than Group B(statistically significant) & also Group C is higher than Group B(statistically significant). Mean Diastolic Bp at 30min of Group A is higher than Group C (statistically significant) & also Group C is higher than Group B

(statistically significant).

		N	Mean	Std. Deviation	P value
pre_pr	Group A	40	78.67	8.06	0.428
	Group B	40	78.80	6.50	
	Group C	40	77.70	5.76	
	Total	120	79.75	7.12	
pr0	Group A	40	77.90	7.84	0.136
	Group B	40	75.40	8.55	
	Group C	40	74.63	6.20	
	Total	120	75.98	7.66	
pr3	Group A	40	74.85	6.84	0.063
	Group B	40	72.28	8.63	
	Group C	40	71.33	4.48	
	Total	120	72.82	6.97	
pr6	Group A	40	73.73	8.45	0.016
	Group B	40	69.55	10.60	
	Group C	40	68.65	4.67	
	Total	120	70.64	8.50	
pr9	Group A	40	71.80	8.99	0.403
	Group B	40	70.20	88.42	
	Group C	40	67.80	3.70	
	Total	120	74.13	51.32	
pr12	Group A	40	72.60	7.29	0.002
	Group B	40	67.95	6.21	
	Group C	40	69.35	3.83	
	Total	120	69.97	6.22	
pr15	Group A	40	73.10	6.39	0.202
	Group B	40	70.85	5.82	
	Group C	40	72.00	4.37	
	Total	120	71.98	5.62	
pr30	Group A	40	73.63	4.90	0.507
	Group B	40	72.55	5.06	
	Group C	40	73.55	3.69	
	Total	120	73.24	4.58	
pr45	Group A	40	75.40	4.92	0.153
	Group B	40	73.60	4.30	
	Group C	40	73.95	3.80	
	Total	120	74.32	4.40	

Tab.30.PR comparison

Dependent Variable			Mean Difference (I-J)	P value
pr6	Group A	Group B	4.18	0.078
		Group C	5.08	0.021
	Group B	Group A	-4.18	0.078
		Group C	0.90	1.000
	Group C	Group A	-5.08	0.021
		Group B	-0.90	1.000

Tab 31.PR at 6min

Dependent Variable			Mean Difference (I-J)	P value
pr12	Group A	Group B	4.65	0.002
		Group C	3.25	0.049
	Group B	Group A	-4.65	0.002
		Group C	-1.40	0.886
	Group C	Group A	-3.25	0.049
		Group B	1.40	0.886

Table.32.PR at 12min

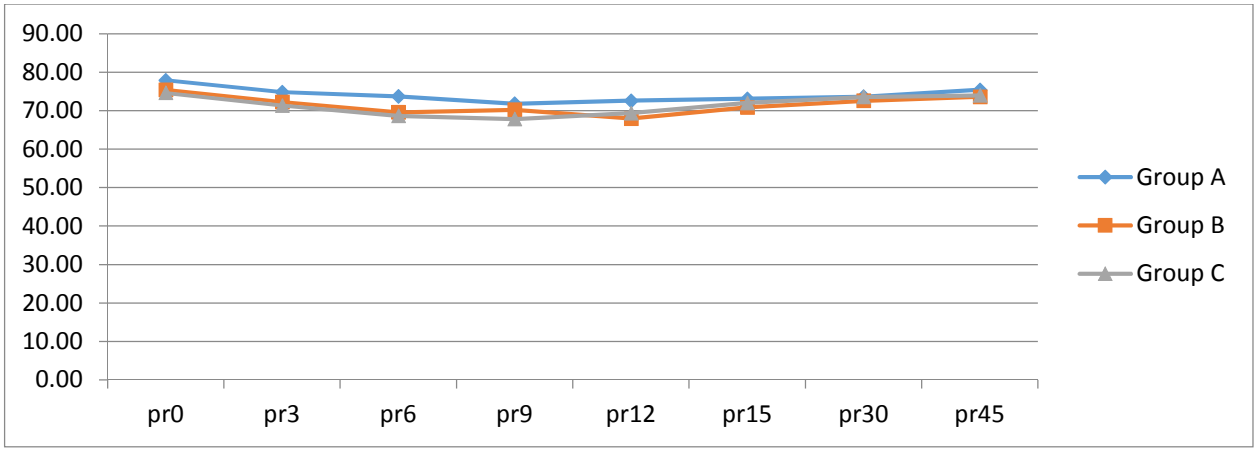

Chart: 15 Comparison of pulse rate

Comparison of pulse rate between three groups at 6min and 12min are statistically significant. Mean pulse rate of Group A at 6min 73/min, at 12min 72/min ,Group B at 6min 69/min,at12min 67/min, and Group C at 6min 68/min, at 12min 69/min.

Spo2	Mean		
	Group A	Group B	Group C
Pre	99.35	99.95	100.00
spo0	100.00	99.35	100.00
spo3	100.00	99.95	100.00
spo6	100.00	99.93	100.00
spo9	100.00	99.93	100.00
spo12	100.00	99.90	100.00
spo15	100.00	99.90	100.00
spo30	100.00	99.90	100.00
spo45	100.00	100.00	100.00

Table.33.Spo2 comparison

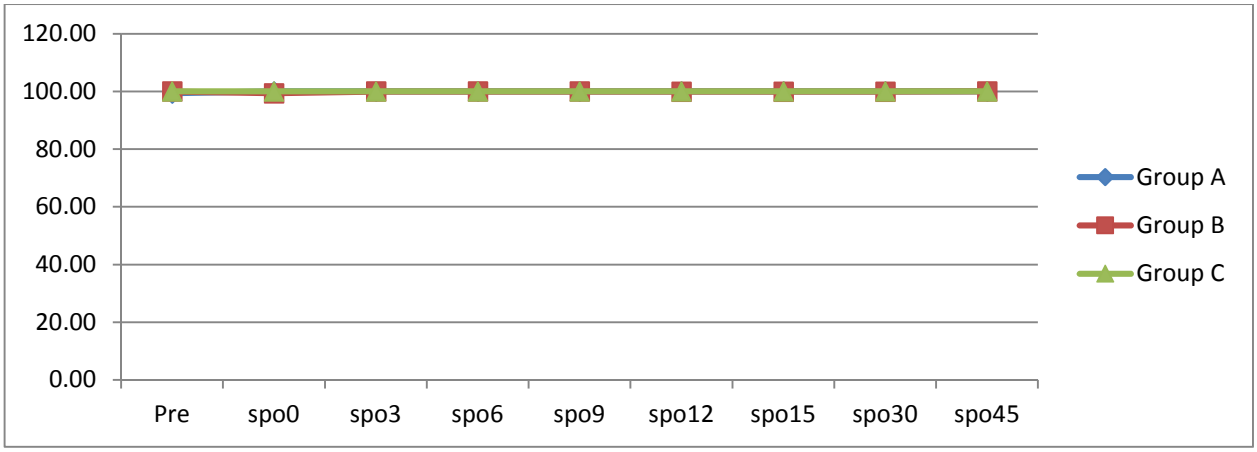

Chart: 16 Comparison of Spo2

Statistically no significance in the comparison of mean Spo2 among three groups.

Postoperative vitals comparison:

		N	Mean	Std. Deviation	P value
postop_sbp					0.012
	Group B	40	117.23	5.12	
	Group C	40	121.50	3.53	
	Total	120	118.56	7.78	
postop_dbp	Group A	40	69.25	3.67	0.047
	Group B	40	69.30	3.75	
	Group C	40	70.95	2.86	
	Total	120	69.83	3.51	
postop_hr	Group A	40	74.80	4.39	0.070
	Group B	40	75.35	3.96	
	Group C	40	76.90	4.17	
	Total	120	75.68	4.24	
postop_spo2	Group A	40	100.00	0.00	n/a
	Group B	40	100.00	0.00	
	Group C	40	100.00	0.00	
	Total	120	100.00	0.00	

Table.34.Post operative vitals comparison

Dependent Variable			Mean Difference (I-J)	P value
postop_sbp	Group A	Group B	-0.27	1.000
		Group C	-4.55	0.024
	Group B	Group A	0.27	1.000
		Group C	-4.28	0.038
	Group C	Group A	4.55	0.024
		Group B	4.28	0.038
postop_dbp	Group A	Group B	-0.05	1.000
		Group C	-1.70	0.089
	Group B	Group A	0.05	1.000
		Group C	-1.65	0.104
	Group C	Group A	1.70	0.089
		Group B	1.65	0.104
postop_hr	Group A	Group B	-0.55	1.000
		Group C	-2.10	0.079
	Group B	Group A	0.55	1.000
		Group C	-1.55	0.299
	Group C	Group A	2.10	0.079
		Group B	1.55	0.299

Tab.35.Postop vitals multiple comparison

Comparing the postoperative vitals among the three groups, the systolic and diastolic Bp are statistically significant with p value 0.012 & 0.047 respectively. PR, spo2 are not statistically significant.

DISCUSSION

Extensive research have been done over the years mainly to improve the quality of spinal anaesthesia simply by varying drug regimens and technical methods. Normally to prolong the anaesthetic effects adjuvants are added to hyperbaric bupivacaine 0.5% and given intrathecally. Adjuvants produce antinociceptive effect by acting perineurally or by acting at different receptor sites in the spinal cord.

Adjuvants mainly opioids are capable of producing early onset of sensory and motor blockade and also prolongs the postoperative analgesia. They also have sympathetic and motor sparing activities which allows early ambulation of patients postoperatively.

Nalbuphine hydrochloride is a mixed μ antagonist and κ agonist opioid. Nalbuphine has been found to cause prolongation of the effects of local anaesthetics in intrathecal, epidural and also in peripheral nerve blocks and it has the advantages of minimal respiratory depression and better hemodynamic stability.

Various studies had been done using 25mcg of fentanyl added to 0.5% hyperbaric bupivacaine which administered intraathecally for various surgeries, including gynaecological surgeries/lower limb surgeries/lower abdominal surgeries/caesarean section and revealed the efficacy and safety of intrathecal fentanyl.

Intrathecal fentanyl and nalbuphine hydrochloride was in practice over many years and found to be safe and effective and has no neurotoxic side effects when used intrathecally.

Mukherjee et al performed a study to determine whether Nalbuphine hydrochloride is safe and whether it helps to prolongs analgesia by comparing it with control group and also to determine the optimum dose of intrathecal nalbuphine'. They observed that 0.4mg of nalbuphine + 0.5% hyperbaric bupivacaine prolongs the duration of postoperative analgesia without any side effects. Hence we used 0.5mg of nalbuphine intrathecally.

Sensory blockade:

In my study, fentanyl significantly shortens the time of onset of sensory block when to compared to nalbuphine. The mean onset time of sensory block (T10) in the nalbuphine group was found to be 3.05±0.88 mins, in fentanyl group it is 2.25±0.63 mins ,whereas in the control group it was found to be 4.08±1.25 mins. In Fentanyl group the mean time of onset of sensory block was 0.80mins earlier than nalbuphine group. Comparison of mean time to reach highest sensory level among three Groups is statistically significant (P value0.002). Time to reach highest sensory level of Fentanyl group was (11.68±2.44 mins) much earlier than nalbuphine Group (13.75±2.06 mins) and it is statistically significant (P value 0.003).Early onset and earlier to reach highest sensory level of

blockade by fentanyl group may be explained due to high lipid solubility of fentanyl which makes it to cross blood brain barrier easily and also rapid tissue uptake. Similar result was obtained by the study conducted by Gurunath BB et al., [39] in 2018 and study conducted by Ravikiran J Thote et al., [33] However the study conducted by Hala Mostafa Gomaa et al., [36] concluded that there is no significant difference between intrathecal nalbuphine and fentanyl regarding to the sensory blockade.

More number of patients in the nalbuphine group (A) achieved higher sensory level (T2 toT4) than the patients in the fentanyl Group(B) (T2 to T5). The mean time for two sement regression of sensory block in the nalbuphine group was found to be 90.40±13.79 mins and in fentanyl group B was 81.35±6.77 mins whereas in the control group it was found to be 50.98±3.58 mins. Higher sensory level and more prolongation of two segment regression of sensory blockade by intrathecal nalbuphine than intrathecal fentanyl was concluded by the studies conducted by Ravikiran J Thote et al., [33] Gurunath BB et al., [39] , Shehla Shakooh et al [30], and by Jyothi B et al., [30].

Motor blockade:

The mean onset time of motor block was found to be 2.33±0.69 mins in the nalbuphine group, 1.48±0.51 mins whereas in the control group it was found to be 3.43±0.93 mins. Similar to sensory blockade the onset of motor blockade is much earlier in fentanyl group than nalbuphine group

just because of highly liphophillic nature of fentanyl. Mean duration of motor blockade in the nalbuphine group was 3.41±0.322 hrs, in the fentanyl group it is3.19±0.747hrs and in the control group was 1.97±0.358 hrs which was statistically significant(p value <0.0001). Mean duration of motor blockade in nalbuphine group is higher than fentanyl group.

Study conducted by Ravikiran J Thote et al., [33] , and the study conducted by Pallavi Ahluwalia et al., [37] concludes similar results. However Hala Mostafa Gomaa et al., [36] concludes that there is no statistically significant difference in the duration of motor blockade between intrathecal nalbuphine and fentanyl.

Duration of analgesia:

The mean duration of analgesia in the nalbuphine group was found to be 5.15±.350 hrs , in fentanyl group was 4.05±.539hrs and in the control group it was found to be 2.64±0.349hrs which was statistically significant (p value <0.0001) between the three groups. The results that obtained in our study reveals that duration of analgesia is much prolonged by intrathecal nalbuphine than fentanyl.

Study conducted by Ravikiran J Thote et al., [33] also concludes that intrathecal nalbuphine prolongs the duration of analgesia than intrathecal fentanyl. Shehla shakooh,et al., [33] study also concludes that sensory blockade ,motor blockade and post operative analgesia was much prolonged with intrathecal nalbuphine group than plain bupivacaine

group. Mukherjee et al., [33]2011 study concluded that 0.4mg nalbuphine is the most effective intrathecal dose that increases postopertative analgesia with no side sffects. Gurunath BB et al., [39] Study also cocludes that the nalbuphine group had much prolonged duration of postoperative analgesia than fentanyl group.

Haemodynamic parameters:

Comparison of mean systolic blood pressure among Group A, Group B, Group C is statistically significant at 0min($p<0.026$),3min($p<0.002$), 6min($P<0.012$), 9min ($p<0.018$) and 45min($p<0.0001$). In multiple comparison the mean SBP of nalbuphine Group A is higher than fentanyl Group B & control group C at 0,3,6,45 min. SBP of Group A is lower than Group B & C at 9min and it is statistically significant($p<0.018$). Comparing the mean diastolic BP of three groups is statistically significant at 6min ($p<0.003$) and 30min ($p<0.004$). In multiple comparison, Mean Diastolic Bp at 6min of Group A is higher than Group B which is statistically significant($p <0.004$) and also Group C is higher than Group B which is statistically significant($p <0.022$). Mean Diastolic Bp at 30min of Group A is higher than Group C (not statistically significant) & also Group C is higher than Group B (statistically significant $p<0.004$). Comparison of pulse rate between three groups at 6min ($p<0.016$) and 12min ($p<0.002$) are statistically significant. Mean pulse rate of Group A at 6min 73/min, at 12min 72/min ,Group B at

6min 69/min,at12min 67/min, and Group C at 6min 68/min, at 12min 69/min.

Comparing the postoperative vitals among the three groups, the systolic and diastolic Bp are statistically significant with p value< 0.012 & < 0.047 respectively. PR, spo2 are not statistically significant. Though statistically significant variation was noted in haemodynamic parameters like non invasive blood pressure(NIBP)/HR/spo2 periodically both intraoperative and postoperative period among the three groups, all patients were haemodynamically stable in all three groups. Intrathecal opioids intensifies the sensory block without increasing sympathetic block just because they are synergistic with local anaesthetics. Our results are similar to the results concluded by Hala Mostafa Gomaa et al study., [36]

Side effects:

Bradycardia and hypotension observed was treatable and it was mainly due to the sympathetic blockade of the local anaesthestics itself and not by the adjuvants added. Shivering was observed more in control group than the nalbuphine group. Side effects observed during our study was very minimal and most of the cases were stable and it is not statistically significant. Various studies conducted concludes the safety and effectiveness of nalbuphine and fentanyl when added intrathecaliy.

SUMMARY

A double blinded randomized controlled study was conducted in 120 patients belonging to ASA I and II undergoing elective hernioplasty surgeries to compare Nalbuphine and Fentanyl given intrathecally with hyperbaric 0.5% bupivacaine for perioperative anaesthesia /postoperative analgesia.

Patients were divided randomly into three groups of 40 each.

Group A received 3 ml 0.5% bupivacaine (15 mg) and 0.5 ml of nalbuphine (0.5 mg).

Group B received 3 ml 0.5% bupivacaine (15 mg) and 0.5 ml fentanyl(25 mcg).

Group C received 3 ml 0.5% bupivacaine (15 mg) and 0.5 ml normal saline.

Equal volume of the solution was injected, 3.5 ml in all the three groups.

Sensory blockade and motor blockade onset time, time to reach maximum sensory level, two segment regression time, the duration of sensory and motor blockade and the duration of analgesia were noted in all the three groups.

Demographic data obtained were similar in all the three groups.

We found that the onset of sensory and motor blockade, time to reach highest sensory level blockade was earlier in the Group B (fentanyl)

than the Nalbuphine Group A. More number of patients to reach highest sensory level blockade was with the Nalbuphine Group A than the Group B (fentanyl) The duration of motor blockade, two segment regression of sensory block, and duration of analgesia was prolonged in the Nalbuphine group than Fentanyl group.

Side effects observed during study was very minimal and most of the cases were stable in all the three groups.

CONCLUSION

Comparing between Intrathecal Nalbuphine and Fentanyl concludes that: Intrathecal Nalbuphine may be a good alternative to Fentanyl in surgeries like hernioplasty and in below umbilical surgeries which provides a prolonged sensory and motor blockade, and prolonged duration of analgesia without any adverse effects.

REFERENCES

1. Lee YY, Muchhal K, Chan CK, Cheung AS. Levobupivacaine and fentanyl for spinal anaesthesia: a randomized trial. Eur J Anaesthesiol 2005;22(12):899–903.

2. Bandi E, Weeks S, Carli F. Spinal block levels and cardiovascular changes during post-cesarean transport. Can J Anaesth 1999;46(8):736–40.

3. Parpaglioni R, Frigo MG, Lemma A, Sebastiani M, Barbati G, Celleno D. Minimum local anaesthetic dose (MLAD) of intrathecal levobupivacaine and ropivacaine for caesarean section. Anaesth 2006;61(2):110–5

4. Brown DL. Spinal epidural and caudal anaesthesia. In: Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish GP, Young WL, editors. Millers' Anaesthesia. 7th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2010.p. 1624.

5. Biswas BN, Rudra A, Bose BK. Intrathecal fentanyl with hyperbaric bupivacaine improves analgesia during caesarean delivery and in early postoperative period. Indian J Anaesth 2002;46:469.

6.Subedi A, Tripathi M, Bhattarai BK, Gupta PK The effect of height and weight adjusted dose of intrathecal hyperbaric bupivacaine for elective caesarean section. J Nepal Med Assoc 2011;51:1-6.

7. Hunt CO, Naulty JS, Bader AM, Hauch MA, Vartikar JV, Datta S, et al. Perioperative analgesia with subarachnoid fentanylbupivacaine for Cesarean delivery. Anesthesiology 1989;71:535-40.

8. Al-Ghanem,SM, Massad IM, Al-Mustafa MM, Al-Zaben KR, Qudaisat IY. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynecological procedure. Amer Jour of Appl Scien. 2009; 6(5): 882-887. (2): 83-95.

9. Akerman B, Arwestrom E, Post C, Local anaesthetics potentiates spinal morphine antinocioception. Anesth Analg1988; 67(10):943-8.

10. Yaksh TL, Rudy TA. Analgesia mediated by a direct spinal action of narcotics. Science 1976;192:1357-8.

11. Wang JK, Nauss LA, Thomas JE. Pain relief by Intrathecally applied morphine in man. Anesthesiology 1979;50:149-51.

12. Veering B. Focus on Adjuvants in regional Anesthesia. Euro Anesthesia 2005;28-31:217-21.

13. Pick CG, Paul D, Pasternak GW. Nalbuphine, a mixed kappa1 and kappa 3 analgesic in mice. J Pharmacol Exp Ther 1992;262:1044-5.

14. BenDavid B, Miller G, Gavriel R, Gurevitch A. Low-dosebupivacaine-fentanyl spinal anaesthesia for caesarean delivery.Reg Anesth Pain Med. 2000 May-Jun;25(3):235-9.

15. A.J.Gissen, L.D.Gugino, Datta S. Effects of fentanyl and sufentanyl on peripheral mammalian nerves. Anaes & Anal 1987; 66(12): 1271-76.

16. Harold Ellis, Anatomy for anaesthetist:9th ed,west Sussex,Blackwell,2014:Part 3: 109-142.

17. Quinn H. Hogan, Anatomy of Neuraxis,in:Micheal J Cousins,Philip o Bridenbaugh,Daniel B Carr,Terese T Horlocker(eds.) Cousins and Bridenbaug's Neural blockade in clinical anaesthesia and painmedicine: 4th ed.Philadelphia, Walters Kluwer & Lippincott Williams and Wilkins,2009, chapter 9: P 181-212.

18.Chaurasia B, ,Contents of vertebral canal,in: Chaurasia B ,Garg K, Mittal P and Chandrupatla M (eds.)B.D, chaurasia's human anatomy:7th ed, New Delhi,CBS publishers ,volume 3; chapter 11: 189-194.

19. David L Brown. Spinal, epidural and caudal Anaesthesia In:Miller RD, editor .Miller's Anaesthesia Volume 2:7th ed.Philadelphia: Elsevier, Churchill Livingstone;2010:1611-35.

20.Pamela Flood,Steven Shafer,Neurophysiology,In:Pamela Flood, James P.Pathmell,Steven Shafer,(eds.)Stoelting's Pharmacology andphysiology in anaesthetic practice,5th ed,Philadelphia,wolters kluwer,2015, chapter 3: 45-197.

21. Hocking G, Wildsmith J A W. Intrathecal Spread. Br J Anaesth2004 ;93(4) : 568-78..

22.Taussig R, Iñiguez-Lluhi JA, Gilman AG. Inhibition of adenylylcyclase by Gi alpha. Science.1993;261:218–221.Dhawan BN, Cesselin F, Raghubir R, Reisine T, Bradley PB,Portoghese PS, Hamon M. International Union of Pharmacology. XII: Classification of receptors. Pharmacol. Rev. 1996;48:567–592

23. Dhawan BN, Cesselin F, Raghubir R, Reisine T, Bradley PB,Portoghese PS, Hamon M. International Union of Pharmacology.XII: Classification of receptors. Pharmacol. Rev. 1996;48:567–592.

24.T.Andrew Bowdle.Pharmacology of analgesia In: Wylie and Churchill Davidson's A practice of anaesthesia.Thomas E J and Paul R Knight; 7th edition.Arnold; 2003:543-63.

25.Kenneth cummings,Mohammed A.Naguib,Opioid Agonists and Antagonists In:Pamela Flood, James P.Pathmell,Steven Shafer,(eds.)Stoelting's Pharmacology and physiology in anaesthetic practice,5th ed,Philadelphia,wolters kluwer,2015, chapter 7:P 217-250.

26. Schmauss C, Doherty C, Yaksh TL. The analgesic effects of an intrathecally administered partial opiate agonist, nalbuphine hydrochloride. Eur J Pharmacol 1982;86:1-7.

27. Penning JP, Samson B, Baxter AD. Reversal of epidural morphineinduced respiratory depression and pruritus with nalbuphine. Can J Anaesth 1988;35:599-604.

28. Romagnoli A, Keats AS. Ceiling effect for respiratory depression by nalbuphine. Clin Pharmacol Ther 1980;27:478-485.

29. Mukherjee A, Pal A, Agrawal J, Mehrota A, Dawar N . Intrathecal nalbuphine as an adjuvant to subarachnoid block:What is the most effective dose? . Anesth Essays Res 2011;5:171-5.

30. Jyothi B, Shruthi Gowda, Safiya Shaikh . A comparison of analgesic effect of different doses of intrathecal nalbuphine hydrochloride with bupivacaine and bupivacaine alone for lower abdominal and orthopedic surgeries. Indian J Pain 2014;28:18-23.

31. Shakooh S, Bhosle P. Intrathecal nalbuphine: An effective adjuvant for post-operative analgesia. Innovative J Med Health Sci2004;4:79-82.

32. Mostafa Galal Mostafa, Mohamad F. Mohamad, Waleed S.H Farrag. Which has greater analgesic effect: Intrathecal Nalbuphine or Intrathecal Tramadol? Journal of American Science 2011;7(7):480-484.

33. Ravikiran J Thote, Prashant Lomate, Shilpa Gaikwad, Jyotsna S Paranjpe, Manohar Mane. Comparison among intrathecal fentanyl

and nalbuphine in combination with bupivacaine and plain bupivacaine for lower limb surgeries. Int J Trends in Science and Technology March 2015;14(2):361-366.

34.Bindra TK,Kumar P,Jindal G.Postoperative Analgesia with Intrathecal Nalbuphine versus Intrathecal Fentanyl in cesarean section:A Double-blind Randomized comparative study.Anesth Essays res.2018 Apr-Jun;12(2):561-565.doi:10.4103/aer.AER_41_18.

35. Chatrath V, Attri JP, Bala A, Khetarpal R, Ahuja D, Kaur S. Epidural nalbuphine for postoperative analgesia in orthopedic surgery. Anesth Essays Res 2015 sep-Dec;9(3):326-30.

36.Hala Mostafa Gomaa, Nashwa Nabil Mohamed, Heba Allah Hussein Zoheir, Mohamad Saeid Ali. A comparison between postoperative analgesia after intrathecal nalbuphine with bupivacaine and intrathecal fentanyl with bupivacaine after cesarean section. Egypt J Anesth. (2014) 30, 405-410.

37. Ahluwalia P, Ahluwalia A, Varshney R, Hakur S, Bhandari S. A prospective randomized double-blind study to evaluate the effects of intrathecal nalbuphine in patients of lower abdominal surgeries under spinal anaesthesia. Int J Sci Stud 2015;3(3);19-23.

39. Gurunath BB, Madhusudhana R.Postoperative analgesic Efficacy of Intrathecal Fentanyl compared to Nalbuphine with Bupivacaine in Spinal Anesthesia for Lower Abdominal surgeries.Anesth Essays res.2018 Apr-Jun;12(2):535-538.doi:10.4103/aer.AER_55_18.

38. Xavier Culebras, Giovanni Gaggero, Jiri Zatloukal, Christian Kern, Rene-Andreas Marti. Advantages of Intrathecal Nalbuphine, Compared with Intrathecal Morphine, After Cesarean Delivery: An Evaluation of Postoperative Analgesia and Adverse Effects Anesth Analg 2000;91:601-5.

40. Moustafa AA, Baaror AS, Abdelazim IA. Comparative study between nalbuphine and ondansetron in prevention of intrathecal morphine -induced pruritus in women undergoing cesarean section. Anesth Essays Res 2016;10:238-44.

41. Gupta R , Varma R , Bogra J, Kohli M, Raman R, Kushwala J K. A comparative study of intrathecal Dexmedetomidine and Fentanyl as adjuvants to Bupivacaine. J Anaesthesiol clin Pharmacol 2011 ;27(3):339-43.

42. HA Nayagam, N Ratan Singh, and H Shanti Singh Indian J Anaesth. 2014 Jul-Aug; 58(4): 430–435.

PATIENT CONSENT FORM

STUDY TITLE

Comparison of Intrathecal Nalbuphine vs Fentanyl added to 0.5% Hyperbaric Bupivacaine for perioperative anaesthesia and perioperative/postoperative analgesia in Hernioplasty.

STUDY CENTRE

TIRUNELVELI MEDICAL COLLEGE AND HOSPITAL, TIRUNELVELI.

PARTICIPANT NAME :

AGE :

SEX :

I confirm that I have understood the purpose of procedure for the above study . I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction. I have been explained about the pitfalls in the procedure. I have been explained about the safety, advantage and disadvantage of the technique.

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason. I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study .

I understand that my identity will not be revealed in any information released to third parties or published , unless as required under the law. I agree not to restrict the use of any data or results that arise from the study. I understood that I will receive drugs to prolong the duration of analgesia using nalbuphine in subarachnoid block. I have been explained that the anesthetic technique is a standard and approved technique. This may help in future research in the field of anesthesia. I consent to undergo this procedure.

INSURANCE NO:

DATE:

Signature / thumb impression of patient

KEY TO MASTER CHART

GROUPS

GROUP A = Bupivacaine + Nalbuphine

GROUP B = Bupivacaine + Fentanyl

GROUP C = Bupivacaine + Normal Saline

PARAMETERS

SOT = sensory block onset time

THSL =time to reach highest sensory block level

TRSL = time for two segment regression of sensory block level

MOT = time of onset of motor block

DMB = duration of motor block

DOA = duration of analgesia

PR = pulse rate

SBP = systolic blood pressure

DPB = diastolic blood pressure

PROFORMA

COMPARISON OF INTRATHECAL NALBUPHINE VS FENTANYL ADDED TO 0.5% HYPERBARIC BUPIVACAINE FOR PERIOPERATIVE ANAESTHESIA AND PERIOPERATIVE / POST OPERATIVE ANALGESIA IN HERNIOPLASTY

Name: Age: ASA PS:

Height: Weight:

Group:

Drug used in SAB:

Pre operative:

BP

PR

SPO2

Intra Operative

	Immediately	3 min	6 min	9 min	12 min	15 min	30 min	45 min	Post op
BP									
PR									
SPO2									

Onset of Sensory Block:

Highest Level of Sensory Block :

Time taken to Reach Highest Level of Sensory Block:

Two Segment Regression of Sensory Level:

Onset of Motor Block:

Duration of Motor Block:

Side Effects:

Duration of Analgesia :

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
(மருத்துவ ஆய்வில் பங்கேற்பதற்கு)

ஆய்வு செய்யப்படும் தலைப்பு:
பங்கு பெறுவரின் பெயர்:
பங்கு பெறுவரின் வயது:

		பங்கு பெறுவர் இதனை ✓ குறிக்கவும்
1.	நான் மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்களை படித்து புரிந்து கொண்டேன். என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன்.	☐
2.	நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.	☐
3.	இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்காள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.	☐
4.	இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.	☐
5.	இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன் எனக்கு கொடுக்கப்பட்டஅறிவுரைகளின் படி நடந்து கொள்வதுடன், ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ, அல்லது எதிர்பாராத, வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்றேன்.	☐

பங்கேற்பவரின் கையொப்பம் / ..... இடம் .....
கட்டைவிரல் ரேகை
பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....
ஆய்வாளரின் கையொப்பம் /..... இடம் .....
ஆய்வாளரின் பெயர் .....
மையம் .....
கல்வியறிவு இல்லாதவற்கு (கைரேகை வைத்தவர்களுக்கு) இது அவசியம் தேவை
சாட்சியின் கையொப்பம் /..... இடம் .....
பெயர் மற்றும் விலாசம் ....

Sl. No.	Name	Age	Sex	Group	Height in CM	Weight in Kg	ASA	Pre Operative				BP mmHg															
								BP mmHg		PR per min	SPO2 %	0 Min		3 Min		6 Min		9 Min		12 Min		15 Min		30 Min		45 Min	
								SBP	DBP			SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
1	Malaiselvam	26	M	A	164	60	I	120	68	72	100	110	70	112	68	108	64	102	68	112	64	108	66	104	66	112	68
2	Udhayakumar	27	M	A	168	72	I	118	70	74	100	112	68	110	66	104	66	102	68	112	70	110	74	108	70	116	72
3	Madasamy	56	M	A	170	70	II	120	74	80	100	114	70	114	68	108	62	100	60	106	64	112	68	116	74	114	68
4	Anantha Kumar	56	M	A	168	69	II	126	82	86	100	120	74	118	70	116	84	108	66	104	62	100	68	110	70	116	74
5	Marimuthu	47	M	A	162	64	II	124	84	90	100	122	78	116	72	114	80	100	74	108	72	118	74	116	70	120	66
6	Shanmuganathan	47	M	A	166	64	II	120	80	94	100	120	80	110	70	110	70	100	70	110	70	120	76	120	74	126	80
7	Arunachalam	51	M	A	168	67	II	122	74	84	100	118	70	116	66	104	64	100	66	102	68	112	66	118	68	118	70
8	Velu	28	M	A	170	72	I	124	76	86	100	120	72	118	68	106	66	96	68	98	70	116	72	116	70	118	74
9	Esakki	54	M	A	162	64	II	126	78	88	100	122	74	120	70	108	68	98	70	100	72	118	74	118	72	120	76
10	Subbiah	56	M	A	165	61	II	128	80	90	100	124	76	118	72	110	70	100	72	110	74	120	76	120	74	122	78
11	Udhayakumar	37	M	A	167	71	I	124	76	84	100	120	68	110	74	104	68	102	62	102	66	110	70	112	72	108	68
12	Shamugam	50	M	A	166	68	II	124	74	78	100	122	68	124	66	118	66	114	64	116	68	108	64	116	68	104	64
13	Ram	39	M	A	165	65	I	122	72	76	100	120	70	122	68	118	64	112	62	114	68	108	62	114	66	102	60
14	Arumugam	22	M	A	164	64	I	130	80	78	100	130	60	130	62	130	62	128	58	134	54	134	58	132	62	136	66
15	Sankara Narayanan	54	M	A	160	58	II	130	90	90	100	128	80	112	70	108	70	113	66	112	60	116	65	119	70	115	70
16	Selvaraj	48	M	A	162	60	II	126	72	90	100	122	70	118	68	110	68	112	70	106	74	112	66	118	68	112	70
17	Arudaiappan	50	M	A	164	63	II	124	78	86	100	120	68	112	64	108	66	108	68	104	70	110	68	118	66	120	66
18	Arunachalam	28	M	A	169	67	I	122	72	74	100	118	64	112	76	106	64	104	60	106	68	110	66	114	70	108	70
19	Mohaned Hajun	52	M	A	167	65	II	128	76	92	100	118	70	108	72	102	64	100	64	104	68	108	66	110	68	104	62
20	Sudalimuthu	35	M	A	168	74	I	128	78	92	100	118	72	110	66	98	64	94	66	88	62	108	66	112	68	110	70
21	Sundarraj	48	M	A	163	62	II	116	78	88	100	116	72	112	70	110	70	104	68	110	70	112	72	114	74	118	72
22	Thangadurai	56	M	A	164	62	II	118	80	90	100	118	74	110	72	112	74	102	70	112	72	110	74	118	76	120	74
23	Chelliah	55	M	A	166	60	II	126	74	86	100	112	74	114	70	110	66	104	70	114	66	110	68	106	68	114	70
24	Kalimuthu	23	M	A	164	60	I	124	70	80	100	110	72	112	68	110	66	106	72	112	64	108	66	104	64	112	64
25	Shanmujaiah	54	M	A	168	70	II	128	78	96	100	116	68	110	66	100	62	96	68	98	60	98	62	100	60	106	64
26	Kannan	32	M	A	164	66	I	130	80	98	100	114	66	108	64	98	60	94	64	96	96	98	58	95	56	100	60
27	Arumugam	39	M	A	168	64	I	122	72	68	100	122	68	120	68	116	70	114	62	114	64	108	64	110	68	104	64
28	Kalimuthu	22	M	A	164	62	I	120	70	66	100	124	70	120	68	118	68	112	60	112	64	108	62	114	66	102	60
29	Kannan	45	M	A	166	62	II	122	70	84	100	120	68	118	64	112	70	116	70	110	68	112	66	114	80	118	76
30	Chellaiah	46	M	A	164	62	II	126	70	72	100	118	68	112	70	108	68	104	64	100	60	88	62	108	68	110	70
31	Petchimuthu	45	M	A	172	70	I	128	74	78	100	120	74	118	76	116	78	114	76	116	78	116	78	122	74	116	76
32	Madasamy	45	M	A	170	68	I	126	72	76	100	118	72	116	74	114	76	112	74	114	76	114	76	120	72	114	74
33	Sankara Narayanan	54	M	A	156	52	II	124	70	74	100	116	74	114	72	112	74	110	72	112	74	112	74	118	70	112	72
34	Chellapandi	49	M	A	158	56	II	122	66	72	100	114	72	112	70	110	72	108	70	114	76	110	72	116	74	110	68
35	Kannan	46	M	A	160	58	II	124	68	74	74	116	74	114	70	110	74	112	72	116	78	112	74	118	76	112	70
36	Chandran	37	M	A	164	60	I	122	68	76	100	118	74	112	68	114	66	108	70	110	68	118	70	114	66	110	74
37	Saravanan	44	M	A	168	64	I	118	72	84	100	114	72	110	68	112	64	108	72	116	74	108	72	116	70	120	70
38	Lakshmanan	54	M	A	158	54	II	120	78	90	100	116	78	112	70	108	70	112	72	106	70	114	72	118	70	120	66

39	Sankaranarayanan	52	M	A	164	60	II	126	76	88	100	114	76	110	70	106	74	110	68	108	66	106	64	112	68	114	68
40	Nallasamy	56	M	A	167	69	II	128	72	86	100	124	70	116	70	104	68	102	66	118	70	112	74	116	70	118	76
41	Ulaganathan	43	M	B	162	59	II	126	70	76	100	120	72	118	70	116	68	114	70	120	68	118	70	118	64	110	68
42	Chelliah	40	M	B	167	68	I	126	70	74	100	120	72	118	68	108	64	110	70	112	68	116	72	118	70	120	72
43	Muthupandi	50	M	B	163	65	I	126	78	86	100	122	70	118	70	116	68	104	62	100	64	110	66	112	68	118	72
44	Kasthurirengan	56	M	B	162	64	II	126	76	90	100	120	72	118	64	108	66	114	66	106	68	100	70	112	72	118	74
45	Sanmuganathan	47	M	B	160	61	I	122	68	78	100	120	64	110	60	108	60	104	62	100	62	114	68	112	66	116	66
46	Sudalaimani	34	M	B	166	63	I	124	70	80	100	120	68	118	64	112	60	116	64	118	60	112	66	110	68	114	68
47	Sankaralingam	50	M	B	162	64	II	116	74	78	100	112	70	114	68	102	66	108	68	112	68	118	70	114	66	110	70
48	Jankishan	42	M	B	168	69	II	126	70	82	100	124	72	110	70	108	66	112	68	110	68	112	70	114	72	120	68
49	Umarkanth	52	M	B	169	70	II	124	74	78	100	122	70	124	80	124	68	120	66	118	76	118	74	116	70	118	70
50	Chandrasekaran	54	M	B	167	64	II	120	76	76	100	118	72	116	70	110	70	108	66	100	60	102	62	110	70	108	68
51	Kangaraj	45	M	B	162	66	I	118	72	70	100	114	70	112	68	110	68	114	60	108	62	110	68	112	66	118	64
52	Chandran	39	M	B	170	74	I	128	76	80	98	130	78	128	84	120	70	120	68	118	78	120	76	112	66	108	58
53	Nambi	54	M	B	166	69	I	112	74	84	100	108	70	102	64	100	60	106	64	110	68	108	66	106	68	110	70
54	Manikandan	60	M	B	160	59	I	116	70	78	100	110	68	108	66	104	68	106	66	110	70	104	64	108	66	112	70
55	Muniyandi	42	M	B	162	64	II	110	68	70	100	106	62	104	60	108	62	110	68	112	64	106	60	110	70	112	68
56	Murugan	42	M	B	164	66	I	126	70	74	100	112	64	106	62	110	64	114	68	114	70	116	66	118	68	114	70
57	Shekmydeen	55	M	B	165	66	II	128	72	70	100	118	70	108	72	100	60	102	62	108	68	110	70	114	72	106	74
58	Alla Pitchai	52	M	B	169	72	I	120	76	78	100	108	74	102	70	106	68	104	70	110	68	116	74	120	70	118	72
59	Ramalingam	50	M	B	164	68	I	122	72	70	100	120	68	116	64	114	68	116	64	118	68	114	64	116	68	120	66
60	Mankain	37	M	B	166	69	I	112	74	76	100	106	68	104	64	108	68	100	60	104	62	108	70	112	68	114	70
61	Karuppasamy	50	M	B	169	70	II	126	78	80	100	112	66	108	64	102	62	104	68	114	70	112	70	118	68	108	70
62	Muthukrishnan	50	M	B	170	74	I	118	74	76	100	108	66	110	68	104	60	112	66	114	72	118	62	116	68	118	70
63	Murugan	32	M	B	168	69	II	112	70	70	100	106	72	108	70	102	64	104	66	110	68	112	66	114	68	120	66
64	Masanam	56	M	B	162	65	I	126	72	78	100	108	70	100	68	104	60	110	68	112	68	118	70	120	68	122	66
65	Kaji Abdulsamak	35	M	B	168	69	II	120	74	80	100	116	72	112	70	108	68	114	64	106	68	118	70	120	68	116	70
66	Gandhumathinathan	60	M	B	166	68	II	120	80	100	100	110	80	98	60	108	59	100	62	95	62	100	60	96	58	106	64
67	Raja	27	M	B	162	64	II	120	90	78	100	120	80	110	70	98	70	100	80	108	70	110	70	112	76	116	64
68	Madasamy	39	M	B	163	65	I	126	70	78	100	110	70	104	56	104	58	106	60	118	64	112	70	114	70	114	76
69	Somu	54	M	B	168	70	II	126	70	80	100	118	64	110	66	106	68	108	68	112	70	114	68	118	70	120	68
70	Ganesan	50	M	B	169	72	II	124	68	78	100	118	68	112	60	114	72	116	68	114	66	108	70	112	72	118	76
71	Baseer Mydeen	22	M	B	170	68	I	120	74	76	100	120	68	114	62	116	66	116	62	108	60	104	62	108	64	106	62
72	Qudrakumar	45	M	B	160	62	II	118	72	74	100	114	70	108	76	102	62	100	60	106	62	116	66	118	70	120	68
73	Sheik Thervath	38	M	B	166	68	I	126	76	70	100	120	70	118	72	108	64	100	62	102	68	108	70	110	60	114	66
74	Chellamuthu	42	M	B	164	66	I	124	78	88	100	112	68	110	64	108	60	110	60	112	66	118	62	114	64	116	68
75	Sathyaraj	30	M	B	165	67	I	120	90	94	100	120	70	122	68	120	66	126	68	124	68	120	70	126	76	124	70
76	Xavier	45	M	B	166	68	I	128	70	86	100	118	76	112	74	108	66	110	70	106	68	112	76	116	78	112	74
77	Vijaya Ragavan	54	M	B	167	69	II	110	70	84	100	110	64	106	66	102	64	108	70	110	72	112	68	114	70	118	72
78	Kannan	48	M	B	156	60	II	120	90	78	100	120	80	110	70	98	70	100	80	108	70	110	70	112	58	106	64
79	Subbiah	54	M	B	169	72	I	120	76	78	100	108	74	102	70	106	68	104	70	110	68	116	74	120	70	118	72
80	Thomas	58	M	B	169	70	II	124	74	78	100	122	70	124	80	124	68	120	66	118	76	118	74	116	70	118	70
81	Jebamani	58	M	C	164	66	II	126	80	68	100	124	78	120	70	122	74	120	70	118	70	124	72	120	72	122	74
82	Chellaiah	52	M	C	165	66	II	128	86	86	100	122	70	120	74	124	70	118	68	110	64	116	70	120	72	122	70

83	Mayandi	28	M	C	170	74	I	124	80	80	100	120	80	118	76	110	70	112	74	118	68	120	70	116	74	120	74
84	Sundarali	21	M	C	167	70	I	130	90	90	100	126	84	120	80	122	80	120	74	126	70	124	72	126	76	128	70
85	Sudalaikumar	55	M	C	163	60	II	120	74	72	100	116	74	114	68	116	64	108	62	110	66	108	64	110	72	118	70
86	Thangaraj	53	M	C	162	59	II	122	76	74	100	118	76	116	70	118	66	110	64	112	68	110	66	112	74	120	72
87	Murugan	56	M	C	166	65	II	118	72	70	100	118	64	116	60	114	62	110	60	112	64	110	68	106	62	110	70
88	Nagarajan	21	M	C	165	66	I	120	70	72	100	112	66	114	62	108	66	110	64	114	68	112	70	118	70	120	72
89	Maheshkumar	40	M	C	166	65	I	118	72	68	100	116	64	114	66	110	62	112	70	108	64	88	62	108	70	118	76
90	Madasamy	36	M	C	169	71	II	116	70	68	100	114	64	112	64	110	60	112	66	108	60	116	70	118	72	120	70
91	Ajith	20	M	C	166	70	I	120	72	76	100	118	70	116	66	110	64	112	64	114	60	116	66	120	70	120	72
92	Aathimoolam	29	M	C	167	65	I	120	72	72	100	118	70	116	68	110	66	112	68	114	66	118	70	116	74	120	70
93	Mayandi	28	M	C	170	68	I	120	72	72	100	120	64	118	66	110	64	112	70	86	62	110	70	112	74	114	70
94	Pattamuthu	56	M	C	162	64	II	124	70	86	100	116	68	106	72	100	68	102	64	106	62	112	64	118	72	120	74
95	Krishnan	48	M	C	162	58	II	124	72	76	100	120	70	120	68	114	64	110	64	108	60	112	60	114	66	118	70
96	Permnath	22	M	C	160	62	I	110	70	76	100	108	64	104	60	100	60	102	64	112	68	110	70	118	70	116	74
97	Kumar	50	M	C	165	67	II	124	76	78	100	120	70	118	72	108	68	110	64	100	66	104	68	118	70	120	70
98	Mariappan	54	M	C	162	64	II	120	72	74	100	118	70	116	68	114	64	112	66	108	70	110	64	116	68	120	76
99	Shaumugavel	52	M	C	166	62	II	120	76	80	100	118	70	116	72	114	70	114	72	108	74	104	66	118	68	120	66
100	Ganesan	52	M	C	160	64	II	120	72	82	100	114	72	112	68	110	70	110	72	106	68	102	62	108	76	118	66
101	Shanmugavel	47	M	C	168	66	I	124	76	86	100	118	76	116	72	114	74	114	76	110	72	106	66	112	80	122	70
102	Areumuganainar	55	M	C	166	64	II	188	70	70	100	116	68	114	64	108	62	110	60	112	62	114	60	118	72	120	70
103	Mohammed Fager	22	M	C	166	64	I	120	72	84	100	118	66	120	70	108	68	110	68	114	70	118	72	120	70	124	68
104	Abdul Rahaf	44	M	C	164	66	I	120	70	72	100	118	70	116	66	110	64	112	62	114	64	120	74	122	76	120	74
105	Gopal	50	M	C	166	62	II	120	72	74	100	118	70	116	66	110	64	112	62	114	64	116	62	120	74	124	70
106	Mariappan	40	M	C	164	62	I	124	70	76	100	120	74	118	74	120	70	114	68	118	72	120	74	124	72	122	74
107	Prabhakaran	30	M	C	160	63	I	120	72	78	100	118	70	116	70	120	72	110	68	112	66	110	70	114	72	118	70
108	Usmail	56	M	C	164	66	II	124	74	80	100	122	70	120	74	118	70	116	72	118	74	114	68	120	70	122	76
109	Subramanian	50	M	C	158	62	II	120	72	78	100	118	64	116	68	110	70	116	72	120	70	118	72	108	74	112	76
110	Nambi	54	M	C	162	64	II	118	76	82	100	110	70	112	72	110	72	108	68	104	68	116	74	118	78	120	70
111	Avadiappan	54	M	C	170	74	II	120	72	80	100	118	70	118	74	116	70	108	72	104	68	110	76	112	70	120	66
112	Swamydas	46	M	C	164	66	I	118	70	78	100	116	68	116	72	114	68	106	70	102	66	108	74	110	68	118	64
113	Victoraj	27	M	C	164	62	I	122	74	82	100	120	72	120	76	118	72	110	74	106	70	112	78	114	72	112	68
114	Gandhirajan	44	M	C	160	58	II	120	72	80	100	118	70	118	74	118	70	110	70	104	68	110	74	110	70	120	66
115	Shanmugavel	55	M	C	162	64	II	122	74	84	100	116	74	114	70	112	72	112	74	108	70	104	64	110	78	120	68
116	Samsudheen	50	M	C	156	58	II	120	70	88	100	118	70	116	72	116	70	110	68	108	64	100	60	118	74	120	70
117	Arumugam	54	M	C	158	60	I	124	74	80	100	120	70	118	70	108	72	100	64	102	66	112	62	118	66	120	70
118	Sudalai	27	M	C	168	70	I	110	76	76	100	106	74	100	70	102	68	86	60	100	64	106	70	110	72	112	70
119	Raja	32	M	C	164	62	I	122	72	84	100	120	70	118	72	112	64	108	66	104	60	110	60	114	62	108	70
120	Santhanaraj	35	M	C	158	62	I	124	70	76	100	110	78	112	70	108	72	100	64	102	66	112	62	118	66	120	70

Intra Operative																	Post Operative				SOT in Min	HSL	THSL in Min	TSRSL in Min	MOT in Min	DMB in Hours	Side Effects	DOA in Hours
PR								SPO2									BP mmHg		PR per min	SPO2 %								
0 Min	3 Min	6 Min	9 Min	12 Min	15 Min	30 Min	45 Min	0 Min	3 Min	6 Min	9 Min	12 Min	15 Min	30 Min	45 Min		SBP	DBP										
68	64	70	66	72	74	70	74	100	100	100	100	100	100	100	100		116	66	76	100	4	T5	12	88	3	03:10	Nil	04:50
70	72	66	62	62	66	70	74	100	100	100	100	100	100	100	100		114	70	70	100	5	T4	16	92	3	03:30	Nil	05:00
76	74	68	62	64	70	76	74	100	100	100	100	100	100	100	100		112	70	78	100	3	T4	12	90	3	03:15	Nil	05:20
80	76	74	70	72	70	74	76	100	100	100	100	100	100	100	100		180	70	72	100	3	T2	15	98	2	03:40	Nil	05:40
86	84	88	76	70	74	76	70	100	100	100	100	100	100	100	100		118	72	74	100	4	T4	12	94	2	03:15	Nil	05:20
92	88	88	90	90	84	74	84	100	100	100	100	100	100	100	100		122	76	82	100	3	T4	15	98	4	03:20	Nil	05:10
72	70	74	72	76	74	70	76	100	100	100	100	100	100	100	100		116	68	74	100	2	T4	10	90	2	03:10	Nil	04:50
78	80	76	72	78	74	72	76	100	100	100	100	100	100	100	100		120	68	74	100	3	T2	14	94	3	03:25	Nil	05:30
84	82	86	86	80	78	74	82	100	100	100	100	100	100	100	100		122	70	78	100	4	T4	12	90	2	03:15	Nil	05:20
86	84	88	88	82	80	76	84	100	100	100	100	100	100	100	100		124	70	80	100	5	T4	18	82	4	195	Nil	05:20
80	72	74	70	66	68	64	70	100	100	100	100	100	100	100	100		110	72	74	100	2	T2	14	102	2	04:10	Nil	05:20
76	68	64	68	70	66	70	72	100	100	100	100	100	100	100	100		116	68	70	100	2	T4	16	102	2	200	Nil	05:40
74	68	66	70	68	64	66	68	100	100	100	100	100	100	100	100		112	60	70	100	3	T4	12	96	3	03:40	Nil	05:30
64	72	61	58	64	60	66	68	100	100	100	100	100	100	100	100		130	68	70	100	3	T2	15	10	2	04:25	Bradycardia	05:50
92	90	94	92	88	88	85	88	100	100	100	100	100	100	100	100		120	60	84	100	2	T2	12	90	3	04:00	Nil	06:10
82	80	74	76	74	68	68	70	100	100	100	100	100	100	100	100		118	66	76	100	2	T2	14	98	2	03:55	Nil	05:30
80	82	76	64	68	72	74	80	100	100	100	100	100	100	100	100		116	72	82	100	3	T4	14	92	2	03:50	Nil	05:15
72	68	64	66	72	76	80	74	100	100	100	100	100	100	100	100		118	68	76	100	3	T4	12	88	2	03:40	Nil	05:10
86	74	78	70	72	76	82	80	100	100	100	100	100	100	100	100		110	70	84	100	3	T4	12	96	2	04:00	Shining	05:15
88	76	80	82	78	74	72	76	100	100	100	100	100	100	100	100		108	72	72	100	3	T4	12	88	2	03:20	Hypertension	05:10
82	80	82	86	86	82	78	76	100	100	100	100	100	100	100	100		118	68	80	100	3	T4	15	88	2	03:15	Nil	05:10
86	84	84	88	86	84	74	82	100	100	100	100	100	100	100	100		120	70	80	100	3	T4	15	90	3	03:25	Nil	05:12
70	72	66	68	68	74	76	74	100	100	100	100	100	100	100	100		118	68	72	100	3	T2	15	96	3	03:45	Nil	05:35
76	74	64	68	64	62	70	72	100	100	100	100	100	100	100	100		114	70	76	100	4	T4	12	94	2	03:35	Nil	05:25
90	78	84	82	80	82	84	76	100	100	100	100	100	100	100	100		108	68	76	100	4	T4	15	88	2	03:25	Nil	05:15
92	78	82	80	80	76	78	78	100	100	100	100	100	100	100	100		102	60	76	100	3	T2	20	85	2	03:40	Nil	05:20
68	64	60	56	68	64	68	68	100	100	100	100	100	100	100	100		108	70	70	100	3	T2	15	98	2	03:50	Bradycardia	05:45
68	64	66	60	58	68	68	66	100	100	100	100	100	100	100	100		108	64	66	100	3	T2	12	95	3	03:45	Bradycardia	05:50
82	80	72	74	76	70	78	74	100	100	100	100	100	100	100	100		120	70	70	100	3	T4	16	92	3	03:15	Nil	05:00
70	68	64	66	70	74	76	78	100	100	100	100	100	100	100	100		112	74	74	100	2	T2	15	96	2	03:50	Hyptension	05:45
76	74	78	72	74	80	78	82	100	100	100	100	100	100	100	100		118	74	76	100	3	T4	12	90	2	03:40	Nil	05:00
74	72	76	70	72	78	76	80	100	100	100	100	100	100	100	100		116	72	74	100	3	T2	15	94	2	03:50	Nil	05:45
72	70	74	68	70	76	74	78	100	100	100	100	100	100	100	100		114	70	72	100	3	T5	14	88	1	03:15	Nil	04:50
70	68	72	66	64	70	74	72	100	100	100	100	100	100	100	100		112	70	70	100	3	T2	12	98	3	03:50	Nil	05:45
66	64	70	72	68	74	70	74	100	100	100	100	100	100	100	100		118	70	76	100	2	T2	15	94	2	03:45	Nil	05:35
70	74	66	68	70	74	68	72	100	100	100	100	100	100	100	100		112	76	68	100	4	T5	12	86	2	3	Nil	04:50
76	72	68	64	70	76	78	72	100	100	100	100	100	100	100	100		116	74	74	100	2	T4	14	94	1	03:15	Nil	05:15
86	84	70	68	74	66	74	78	100	100	100	100	100	100	100	100		112	68	78	100	3	T4	12	92	2	03:40	Nil	05:10

74	70	68	70	72	66	68	74	100	100	100	100	100	100	100	100	110	68	70	100	5	T5	15	90	3	03:20	Nil	04:05
82	80	74	66	68	72	76	74	100	100	100	100	100	100	100	100	120	70	78	100	1	T4	10	90	1	03:25	Nil	04:50
70	72	68	64	66	74	76	78	100	100	100	100	100	100	100	100	112	68	80	100	2	T5	12	80	1	03:15	Nil	04:40
70	72	76	68	62	62	76	70	100	100	100	100	100	100	100	100	122	70	76	100	2	T4	15	84	1	03:20	Nil	04:00
80	82	68	62	64	66	70	72	100	100	100	100	100	100	100	100	120	70	76	100	2	T4	12	86	1	03:30	Nil	04:25
82	76	72	64	62	66	74	78	100	100	100	100	100	100	100	100	118	78	82	100	3	T5	16	75	2	02:50	Nil	03:55
72	70	66	72	76	74	78	72	100	100	100	100	100	100	100	100	118	68	74	100	2	T2	15	92	2	03:10	Nil	04:00
76	70	64	68	66	76	72	74	100	100	100	100	100	100	100	100	118	70	76	100	1	T4	14	88	1	03:40	Nil	04:20
80	82	76	66	64	62	70	76	100	100	100	100	100	100	100	100	112	76	76	100	2	T5	12	78	2	03:15	Nil	04:15
78	74	62	64	68	70	74	72	100	100	100	100	100	100	100	100	122	70	76	100	1	T4	10	86	1	03:20	Nil	04:40
74	72	64	68	70	72	76	78	100	100	100	100	100	100	100	100	118	68	82	100	2	T4	10	80	2	03:00	Nil	04:10
70	72	66	68	64	62	66	74	100	100	100	100	100	100	100	100	112	64	70	100	2	T5	8	84	1	04:00	Nil	04:30
68	66	64	62	68	70	72	74	100	100	100	100	100	100	100	100	120	70	78	100	2	T5	16	78	1	03:10	Nil	03:45
68	73	60	626	62	60	56	58	98	98	97	97	96	96	96	100	110	60	68	100	2	T4	10	88	2	03:20	Bradycardia	04:20
76	74	72	76	68	66	70	74	100	100	100	100	100	100	100	100	118	68	78	100	3	T4	10	82	2	02:50	Nil	04:20
70	64	68	66	62	64	70	72	100	100	100	100	100	100	100	100	114	68	70	100	2	T5	12	80	1	03:15	Nil	04:00
68	64	70	72	70	76	74	72	100	100	100	100	100	100	100	100	117	70	72	100	1	T4	12	78	2	03:00	Nil	04:10
70	66	72	68	74	70	72	76	100	100	100	100	100	100	100	100	116	72	78	100	2	T2	10	92	1	04:10	Nil	04:50
68	64	60	68	70	72	76	70	100	100	100	100	100	100	100	100	108	76	74	100	3	T4	8	86	2	03:00	Nil	04:15
76	70	64	68	70	74	70	76	100	100	100	100	100	100	100	100	122	68	78	100	2	T5	15	78	1	02:45	Nil	03:20
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76	74	70	68	74	66	70	76	100	100	100	100	100	100	100	100	116	74	78	100	3	T3	10	96	2	03:40	Nil	05:10
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68	64	70	76	68	70	72	76	100	100	100	100	100	100	100	100	118	70	72	100	2	T5	10	76	1	02:45	Nil	03:20
76	70	64	68	66	72	74	78	100	100	100	100	100	100	100	100	128	74	76	100	1	T4	12	76	1	03:10	Nil	04:40
76	70	72	76	70	76	70	72	76	100	100	100	100	100	100	100	118	72	76	100	3	T5	10	80	2	03:25	Nil	05:00
106	102	110	96	87	86	83	76	100	100	100	100	100	100	100	100	106	64	76	100	3	T5	10	82	2	6	Hypotension	05:00
68	64	60	62	60	68	70	74	100	100	100	100	100	100	100	100	116	64	74	100	3	T3	8	60	2	03:30	Bradycardia	02:30
70	60	58	56	60	72	76	74	100	100	100	100	100	100	100	100	118	70	72	100	3	T4	10	80	2	03:10	Bradycardia	04:15
76	72	68	70	66	74	72	76	100	100	100	100	100	100	100	100	122	70	78	100	2	T5	12	78	1	02:50	Nil	03:45
76	68	64	66	70	74	72	74	100	100	100	100	100	100	100	100	120	68	76	100	3	T4	14	80	2	03:10	Nil	04:20
74	70	76	72	68	66	70	74	100	100	100	100	100	100	100	100	116	70	70	100	3	T4	10	86	2	03:15	Nil	04:20
72	70	68	66	70	74	76	70	100	100	100	100	100	100	100	100	118	68	72	100	2	T5	15	78	1	03:00	Nil	04:10
68	72	66	64	62	70	72	70	100	100	100	100	100	100	100	100	118	60	76	100	2	T4	12	82	1	02:50	Nil	03:45
80	72	74	68	64	76	78	74	100	100	100	100	100	100	100	100	118	70	76	100	2	T5	12	76	1	03:00	Nil	04:10
88	86	80	62	58	64	60	60	100	100	100	100	100	100	100	100	130	70	66	100	2	T4	15	68	1	03:20	Bradycardia	04:10
80	76	64	68	70	76	70	72	100	100	100	100	100	100	100	100	120	68	78	100	2	T4	12	84	1	03:10	Nil	04:12
78	70	66	72	70	68	76	74	100	100	100	100	100	100	100	100	120	70	70	100	3	T5	10	86	2	03:00	Nil	04:15
106	102	110	96	87	86	83	76	100	100	100	100	100	100	100	100	106	64	76	100	3	T5	10	85	2	6	Hypotension	05:00
76	70	64	68	70	74	70	76	100	100	100	100	100	100	100	100	122	70	78	100	2	T5	12	78	1	02:50	Nil	03:45
74	72	64	68	70	72	76	78	100	100	100	100	100	100	100	100	120	68	78	100	3	T4	8	86	2	03:00	Nil	04:15
66	64	62	66	60	68	64	68	100	100	100	100	100	100	100	100	124	70	70	100	05:30	T6	16	52	7	02:20	Nil	02:45
80	74	76	64	68	76	74	78	100	100	100	100	100	100	100	100	124	70	82	100	04:30	T5	12	52	4	02:20	Nil	03:10

76	78	70	68	72	74	72	76	100	100	100	100	100	100	100	100	124	70	78	100	4	T6	15	52	5	02:40	Nil	03:15
92	84	80	70	68	74	68	84	100	100	100	100	100	100	100	100	126	72	86	100	3	T6	15	55	3	02:35	Nil	03:30
70	68	70	66	64	62	74	70	100	100	100	100	100	100	100	100	118	72	72	100	4	T5	12	50	2	02:15	Nil	03:10
72	70	72	68	66	64	76	72	100	100	100	100	100	100	100	100	120	70	74	100	6	T6	18	55	3	02:40	Nil	03:15
68	66	70	64	66	68	70	72	100	100	100	100	100	100	100	100	116	72	74	100	6	T6	1	48	3	02:00	Nil	02:45
70	74	76	68	64	66	74	70	100	100	100	100	100	100	100	100	122	70	78	100	5	T6	16	45	3	01:45	Shining	02:50
66	68	72	70	74	64	66	78	100	100	100	100	100	100	100	100	120	74	84	100	4	T4	16	50	4	02:50	Hypotension	03:00
64	66	68	62	62	64	68	70	100	100	100	100	100	100	100	100	120	72	74	100	5	T6	15	52	3	02:40	Nil	02:55
72	68	70	74	76	74	78	72	100	100	100	100	100	100	100	100	124	70	76	100	4	T6	12	52	4	01:45	Nil	02:40
70	68	68	66	72	74	76	78	100	100	100	100	100	100	100	100	122	70	80	100	4	T6	15	45	4	02:10	Nil	02:45
70	74	72	68	66	70	74	80	100	100	100	100	100	100	100	100	118	82	82	100	5	T6	12	52	4	01:45	Shining	02:15
80	76	64	66	70	72	68	70	100	100	100	100	100	100	100	100	118	72	76	100	5	T6	12	48	4	01:50	Nil	02:45
76	74	68	70	72	66	68	68	100	100	100	100	100	100	100	100	120	70	70	100	5	T6	16	52	4	02:00	Nil	02:45
74	70	72	74	70	72	76	76	100	100	100	100	100	100	100	100	118	70	74	100	4	T5	18	56	3	02:40	Nil	03:10
74	70	62	68	66	70	72	74	100	100	100	100	100	100	100	100	124	70	70	100	5	T6	15	50	4	02:00	Nil	02:50
70	68	72	64	66	68	72	74	100	100	100	100	100	100	100	100	126	70	78	100	4	T6	12	45	2	02:10	Nil	02:50
78	70	66	64	70	74	72	70	100	100	100	100	100	100	100	100	122	70	74	100	4	T6	20	45	4	01:50	Nil	02:35
80	70	66	68	70	74	72	76	100	100	100	100	100	100	100	100	120	64	70	100	6	T6	18	52	5	02:20	Shining	03:10
84	74	70	72	74	78	76	74	100	100	100	100	100	100	100	100	126	70	76	100	4	T6	15	48	3	02:10	Nil	02:45
68	66	64	68	66	70	76	74	100	100	100	100	100	100	100	100	124	70	78	100	3	T5	10	50	3	02:00	Nil	03:10
78	76	78	70	68	74	72	70	100	100	100	100	100	100	100	100	126	70	76	100	5	T6	12	48	4	01:50	Nil	02:45
70	72	68	64	70	72	76	74	100	100	100	100	100	100	100	100	122	70	70	100	4	T6	18	60	4	02:20	Nil	03:00
70	68	66	70	68	72	78	76	100	100	100	100	100	100	100	100	126	70	76	100	4	T6	15	55	4	02:15	Nil	02:50
74	70	72	68	70	74	76	74	100	100	100	100	100	100	100	100	120	76	78	100	4	T6	12	54	3	02:10	Nil	02:30
74	70	58	68	70	74	76	70	100	100	100	100	100	100	100	100	120	70	74	100	03:30	T5	15	53	3	01:50	Bradycardia	02:30
76	74	68	72	66	70	76	74	100	100	100	100	100	100	100	100	124	70	78	100	4	T6	12	51	3	02:00	Nil	02:45
75	66	70	74	76	72	68	70	100	100	100	100	100	100	100	100	118	70	74	100	3	T6	10	48	3	01:30	Nil	02:15
80	74	68	70	74	76	80	84	100	100	100	100	100	100	100	100	120	76	80	100	5	T6	12	52	3	02:00	Nil	03:00
76	70	64	66	72	78	76	74	100	100	100	100	100	100	100	100	124	70	82	100	3	T6	8	48	2	01:50	Nil	02:48
74	68	62	64	70	76	74	72	100	100	100	100	100	100	100	100	122	68	80	100	4	T6	12	50	3	02:15	Nil	02:50
82	72	66	68	74	80	78	76	100	100	100	100	100	100	100	100	126	72	84	100	5	T5	15	45	2	02:30	Nil	03:00
80	70	64	66	72	76	78	74	100	100	100	100	100	100	100	100	122	70	80	100	4	T6	10	52	3	02:40	Nil	03:15
82	72	68	70	72	76	76	76	100	100	100	100	100	100	100	100	124	68	78	100	5	T6	8	55	3	01:55	Nil	02:50
80	82	76	68	64	70	76	78	100	100	100	100	100	100	100	100	122	76	80	100	4	T5	16	58	3	02:15	Nil	02:10
78	76	70	76	74	74	72	76	100	100	100	100	100	100	100	100	120	68	78	100	5	T6	12	52	4	02:00	Nil	02:50
74	70	68	66	68	76	74	72	100	100	100	100	100	100	100	100	114	70	76	100	4	T5	12	54	3	02:20	Nil	03:12
82	78	66	68	72	70	74	70	100	100	100	100	100	100	100	100	110	74	74	100	4	T6	15	50	3	01:50	Nil	02:45
60	65	64	56	72	78	76	74	100	100	100	100	100	100	100	100	124	70	82	100	3	T6	8	48	3	01:50	Bradycardia	02:30